DLPE 8-21-03

1 of 3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Polyakov, I. et al	Art Unit:	1645
Serial No.:	10/085,703	Examiner:	N. M. Minnifield
Filed:	02/28/2002		
For:	Dermatomycosis Vaccine		
Docket:	3/400-4-C4		

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Linda 9/29/03

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Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL FROM THE PRIMARY EXAMINER'S DECISION TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Pursuant to the provisions of 35 U.S.C. § 134 and 37 C.F.R. § 1.191, applicants (hereinafter "appellants") respectfully appeal from the Primary Examiner's final rejection of all of the pending claims. A Notice of Appeal was timely filed on April 15, 2003. It is hereby requested that the time for filing this Appeal Brief be extended pursuant to 37 CFR 1.136(a) for two months, so that the extended period filing this Appeal Brief will end on August 15, 2003. Authorization is hereby given to charge the fee due under 37 C.F.R. § 1.17(c) to Deposit Account No. 02-2955, which is indicated by the enclosed Fee Transmittal Form (Form PTO/SB/17). If it is determined, however, that any additional fees under 37 C.F.R. §§ 1.16 or 1.17 are due in connection with this Appeal Brief, authorization is hereby given to charge such fees to Deposit Account No. 02-2955. This Appeal Brief is being filed in triplicate as required under 37 C.F.R. § 1.192(a).

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REAL PARTY IN INTEREST

09/25/2003 LHUMES 00000001 022955 10085703
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The real party in interest is Boehringer Ingelheim Vetmedica GmbH, Binger Str. 173, 55216 Ingelheim am Rhein, Germany.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any other currently pending appeal or interference that would directly affect, be affected by, or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

The instant application was filed with claims 1 and 2. Claims 1 and 2 are the subject of this appeal and set forth in the Appendix to this Appeal Brief.

STATUS OF AMENDMENTS

No amendments have been filed.

SUMMARY OF INVENTION

The instant claimed invention relates to two dermatomycosis vaccines comprising inactivated dermatophytes, wherein the inactivated dermatophytes **consist** of either eight or three specified dermatophyte strains, all of which were deposited according to the Budapest Treaty.

ISSUE PRESENTED FOR REVIEW

Whether claims 1 and 2 comply with 35 U.S.C. § 112, first paragraph.

GROUPING OF CLAIMS

Each of the two claims stand or fall independently as each claim provides different scope. Appellants therefore request that the Board independently consider the enablement of each claim in light of the arguments below.

ARGUMENT

Appellants respectfully maintain that claims 1 and 2 comply with 35 U.S.C. § 112, first paragraph, in all respects by enabling one of skill in the art to which the invention pertains to make and use the invention, as explained below. Unless indicated otherwise, all of the citations to "Office Action" below are references to the last Office Action dated February 5, 2003.

Copies of the cited Unpublished Board Opinions are enclosed for the Board's convenience. Such Unpublished Board Opinions are cited to show only the proper legal analysis and are acknowledged not to be binding precedent of the Board.

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to

enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (Office Action, page 2).

In response, appellants respectfully traverse the Examiner's rejection and maintain that the claims comply with 35 U.S.C. § 112, first paragraph, and all other statutory requirements in all respects.

In making this rejection, the Examiner has made many unsubstantiated allegations. Appellants will address each allegation made by the Examiner in order and explain why they are each either factually incorrect, legally irrelevant or improper, or both.

A. The Scope of the of Claims under Appeal

> "Where, as here, the issues presented for review concern the practical utility of the full scope of the subject matter claimed and the specification's capacity to enable one skilled in the art to make and use the full scope of the subject matter claimed, claim interpretation is a necessary prerequisite to resolution of the merits presented." (*In re Steele*, 134 U.S.P.Q. 292, 295 (CCPA 1962); *Ex parte Beck*, Appeal No. 94-3222, page 4 (UNPUBLISHED; Exhibit A); emphasis added).

Only the inventions defined by the claims need be explained in the patent application in a manner sufficient to be supported as required by 35 U.S.C. § 112, first paragraph (*Engel Industries, Inc. v. Lockformer Co.*, 20 U.S.P.Q.2d 1300, 1302 (Fed. Cir. 1991).

The claims as presented here for review each include the following clauses:

- "A dermatomycosis vaccine comprising inactivated dermatophytes": this clause indicates that the vaccine may, but does not necessarily have to comprise, in addition to the dermatophytes as specified *infra*, carriers, excipients, adjuvants etc. acceptable for and common in veterinary use as disclosed in the present specification.
- "wherein the inactivated dermatophytes **consist** of:" and listing by accession number either eight or three specified dermatophyte strains, each of which were deposited according to the Budapest Treaty. This part of the claim clearly points out that the

dermatophyte element of the vaccine as claimed is composed of only the deposited strains, see discussion *infra*.

The transitional phrase "consisting of" is close-ended and excludes any element, step, or ingredient not specified in the claim. See M.P.E.P. at § 2111.03; *In re Gray*, 11 U.S.P.Q. 255 (CCPA 1931); *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (Bd. App. 1948). When the phrase "consists of" appears in a clause of the body of a claim, rather than immediately following the preamble, it limits only the element set forth in that clause, other elements are not excluded from the claim as a whole. See M.P.E.P. § 2111.03; *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 230 U.S.P.Q. 45 (Fed. Cir. 1986).

Thus, claim 1 must be interpreted to include no less and no more than the following dermatophytes:

- *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277)
- *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279)
- *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278)
- *Trichophyton equinum* Strain No. VKPGF-929/381 (accession No. DSM 7276)
- *Microsporum canis* Strain No. VKPGF-928/1393 (accession No. DSM 7281)
- *Microsporum canis var. obesum* Strain No. VKPGF-727/1311 (accession No. DSM 7280)
- *Microsporum canis var. distortum* Strain No. VKPGF-728/120 (accession No. DSM 7275)
- *Microsporum gypseum* Strain No. VKPGF-729/59 (accession No. DSM 7274).

Similarly, claim 2 must be interpreted to include no less and no more than the following dermatophytes:

- *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277)
- *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279)
- *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278).

B. Appellants Have Taught How to Make the Vaccines within the Scope of the Claims

This fact is undisputed by the Examiner:

> "The Examiner agrees that the specification teaches how to make the claimed vaccine" (Office Action at page 3, last paragraph).

C. Appellants have Taught how to Use the Vaccines within the Scope of the Claims

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement". *In re Wright*, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993)(emphasis added). See also *In re Morehouse*, U.S.P.Q. 29, 32 (CCPA 1976); *Ex parte Charoenvit*, Appeal No. 1999-1413 (UNPUBLISHED; Exhibit B). The Examiner's conclusory statement "The rejection is maintained for the reasons of record" only accompanied by unsupported allegations not relating to the present claims does not satisfy this burden.

Upon careful review of the previous Office Action dated May 30, 2002, no proper explanation or sufficient reasons were given by the Examiner as to why the scope of protection provided by the claim is allegedly not enabled by the specification.

As no sufficient reasons can be found in either one of the Office Actions, the Office Actions regarding the parent application 09/256,915, to which benefit is claimed in the subject application, were reviewed. Quite surprisingly, the same examiner acknowledged the enablement for the use of the inactivated strain in a vaccine composition:

> "Claim 18, 21-23, 34 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for use of the inactivated strain**, does not reasonably provide enablement for one antigen from the dermatophytes, T. verrucosum, to be used in the vaccine composition." (Final Office Action dated August 29, 2003, page 3 at 6.; emphasis added)

Appellants fully agree with Examiner's conclusion that the specification is fully enabling for the use of any of the inactivated strains. Accordingly, if the use of a vaccine containing only one inactivated strain is considered to be disclosed in an enabling manner, how can the use of a vaccine containing eight or three of such strains not be considered to be disclosed in an enabling manner?

In short, if a vaccine comprising one strain is shown to provide immunity and to comply with the requirements of 35 U.S.C. 112, first paragraph, why should a vaccine comprising several of said strains not provide immunity?

The Examiner put forward several, unsupported allegations as discussed below:

(a) "It is not clear what Applicants used in the vaccine composition. Example 1, page 18 indicates that "[A]fter 2 days, 125 ml of each culture in suspension is taken and mixed in a single container. The vaccine may be prepared by mixing together various combinations of the given strains." Exactly what was the composition of the vaccine administered that gave the results found in Tables 9 and 10? It is not clear if all 8 dermatophytes were used or some combinations of 3, 4, 6 or 7 dermatophytes. It is not clear that the specific combination of 3 dermatophytes as set forth in claim 2 were used." (Office Action at page 2, 4. to page 3, first paragraph).

(b) "Specifically, the specification has not taught how to use the claimed vaccine. Mixing each culture in a single container or mixing together various combinations of the given cultures is set forth. However, it is not clear which composition (all 8 cultures in one container or various combinations of less than 8 cultures and if less than 8 cultures specifically which ones) was used to generate the data found on tables 9 and 10 of the specification." (Office Action at page 3, last paragraph to page 4, first paragraph).

(c) "Does Applicant intend for "immunogenic response" to mean that vaccine protection has been established, see page 11?" (Office Action at page 3, first paragraph). "Does the vaccine comprising a combination of cultures protect in the same manner as the individual cultures; is there a synergistic affect with regard to protection against ringworm infection?" The Examiner further cites Gudding et al (Can. Vet. J. 1995) and continues "Further, the inactivated vaccine against ringworm must be capable of eliciting both humoral and cellular immune responses, of which the cellular immune response is crucial for protection and adjuvants are important in stimulating the cellular branch of the immune system (pp. 303-304). In view of the state of the art it is not clear if protection has been established against ringworm infection when Applicants state (see tables 1-7) "establishes immunity". It is not clear what type of immunity is established. Applicant's vaccine composition does not recite a carrier or adjuvant, however Gudding indicates that the adjuvants are important in stimulating the cellular branch of the immune system and the cellular branch is crucial for protection.

Allegation (a)

With regard to allegation (a), the Examiner has cited only part of Example 1. Omitted is the preceding paragraph:

> "To produce 1 liter of vaccine, cultures are taken of the strains VKPGF-931/410, 930/1032, 929/381, 551/68, 928/1393, 727/1311, 728/120, and 729/59 and grown in agar/wort at 26°C for 15 days. Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer. The solution used is an aqueous solution containing 1% fermented hydrolyzed muscle protein, 10% glucose and 1% yeast extract. The concentration of microconidia is brought to 90 million per ml of homogenate. After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container." (emphasis added).

Therefore, from the quoted wording, it is clear to the skilled person that in cited Example 1 the 8-fold vaccine, exactly as claimed in claim 1, was prepared and used in prophylaxis and therapy.

The sentence "The vaccine may be prepared by mixing together various combinations of the given strains" (emphasis added), uses the term "may" which clearly indicates to the skilled person what optionally may be done, e.g. instead of eight claims, the combination of three strains as recited in claim 2 may be used in a vaccine according to the invention.

Allegation (b)

Regarding allegation (b), the wording of example 1 clearly states that each of the eight cultures is first cultured separately and homogenized:

> "Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer."

and then combined into one container:

> "After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container."

Further, the specification extensively describes immunizing the animals using the vaccine prepared in Example 1 to determine dosage to be given and the method of administration for prevention and treatment in ten different animal families (page 18, line 33 and Table 8). The effectiveness of the vaccine in preventing disease in 24 animal species is given (Example 2, page 21, and Table 9); and the effectiveness of the vaccine in treating infected animals in 18 different animal species is provided (Example 3, page 21 and Table 10).

Furthermore, clarification can also be drawn from page 3, lines 5-12 and 20-22 disclosing preferred vaccine combinations in the context of page 4, lines 8-18:

Page 3, lines 5-12:

> This aim has been achieved by using the following fungal strains as vaccinal strains: *Trichophyton verrucosum* (especially No. VKPGF-931/410), *Trichophyton mentagrophytes* (especially No. VKPGF-930/1032), *Trichophyton equinum* (especially No. VKPGF-929/381), *Trichophyton sarkisovii* (especially No. VKPGF-551/68), *Microsporum canis* (especially No. VKPGF-928/1393), *Microsporum canis var. obesum* (especially No. VKPGF-727/1311),

Microsporum canis var. distortum (especially No. VKPGF-728/120), *Microsporum gypseum* (especially No. VKPGF-729/59). Vaccines can be produced by using various combinations of antigenic material from the above strains together with a suitable carrier.

Page 3, lines 20-22:

"Another preferred combination of vaccine strains consists of *Trichophyton verrucosum* No. VKPGF-931/410, *Trichophyton mentagrophytes* No. VKPGF-930/1032, *Trichophyton sarkisovii* No. VKPGF-551/68, particularly for use in cattle."

Page 4, lines 8-18:

In order to prepare a vaccine the following procedure may be used, for example:

Cultures of the strains are homogenized in an aqueous solution containing 0.2 ti 2.0% fermented, hydrolyzed muscle protein (FGM-s), 5 to 12% glucose and 0.1 to 1.2% yeast extract. The concentration of the microconidia is adjusted to 40 to 120 million per milliliter and after 1 to 2 days the mixture is inactivated, *e.g.*, with thiomersal ($C_9H_9O_2SNaHg$) in the ration 1:10,000 to 1:25,000, or with another substance known from the prior art. The resulting suspension is packaged and is ready for use in animals.

The preparation of the vaccines, the dosage to be given and the method of administration for prevention and therapeutic treatment are explained in Examples 1 to 3.

With the before-mentioned extensive guidance provided to the skilled person, appellants have shown how to make and use both vaccines within the scope of the claims, including claim 2.

Furthermore, the Examiner did not consider and apply the factors and analysis of *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) and *Ex parte Forman*, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). In properly considering and applying the factors concerning enablement, the following factors should be considered: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

With regard to factors (1) and (2), to practice the invention, either 8 or 3 dermatophytes must be grown, mixed together in a single container, the mixture is inactivated, and the resulting vaccine is bottled (described in the specification on pages 4, lines 10-18, page 18, lines 15-31), and applied to animals at a dosage and with a route of administration as disclosed in Example 2, page 21, and Table 9 (prevention) as well as Example 3, page 21 and Table 10 (therapy). As set out *supra*, the dosage and route of administration is given for 10 different animal families, and guidance regarding efficacy of the 8-fold vaccine is given for 24 animal species (prevention) and 18 animal species (therapy) all of which represents a very limited amount of routine experimentation under a significant amount of guidance presented in the specification. If at all, there is minimal routine experimentation necessary to test the 3-fold vaccine in a similar manner as the 8-fold vaccine. With regard to factor (3), there are several in-depth working examples disclosing the preparation of vaccines according to the invention, the dosage, the route of preventive or therapeutic administration for numerous animal species. With regard to factors (4), (5), (6), and (7), as the nature of the invention is in the immunology, animal health and vaccine art, which is very highly developed, the state of the prior art is high, and the relative skill of those in the art is at a very high level, one would expect one of skill in the art would easily be able to use the directions in the specification to make and use the vaccines according to the invention. Regarding factor (8), it should be pointed out again that the claims presented for review are not generic claims, but are directed to two specific vaccines consisting of eight or three specified dermatophytes.

This situation is in contrast to that of *Ex parte Forman*, where the art was "undeveloped", that at the time (early 1980s) "experiments in genetic engineering produce, at best, unpredictable results", there were no apparent reproducible working examples presented outside the scope of the deposited microorganism strains, nor did there "appear to be ... a single detailed example that could be followed by another worker in another lab to obtain a single specific microorganism (vaccine) within appellants' claims, without recourse to the deposited strains recited in the allowed claims." *Ex parte Forman*, at 548. The instant situation is more like *In re Wands*, where enablement was shown, as appellants' disclosure, like Wands' disclosure, "provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *In re Wands* at 1406.

35 U.S.C. § 112, first paragraph, certainly does not require each and every embodiment of the invention to be exemplified. Even the lack of a working example (quite contrary to the situation here with several working examples), if all the other factors point to enablement, is not considered to render the invention non-enabled, if one skilled in the art will be able to practice it without an undue amount of experimentation (M.P.E.P. 2164.02; *In re Borkowski*, 164 U.S.P.Q. 642, 645 (CCPA 1970).

Further, the test is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue (M.P.E.P. § 2164.01; *In re Angstadt*, 190 U.S.P.Q. 214, 219 (CCPA 1976); *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, U.S.P.Q. 409, 413 (Fed. Cir. 1984).

The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *The Johns Hopkins University v. Cellpro Inc.* 47 U.S.P.Q.2d 1705, 1719; *PPG Indus., Inc. v. Guardian Indus. Corp.* 37 U.S.P.Q.2d 1618, 1623 (emphasis added).

With the significant amount of guidance presented in the specification, the minimal routine experimentation necessary to test the 3-fold vaccine in a similar manner as the 8-fold vaccine can certainly not be considered undue.

Allegation (c)

With regard to allegation (c), appellants cite Taber's cyclopedic medical dictionary, in existence since 1940 and clearly the standard to the skilled person (Exhibit C). It is appropriate to compare the meaning of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. *In re Barr*, 170 U.S.P.Q. 330 (CCPA 1971).

"Vaccine" is defined to be used as follows:

> "FUNCTION: Vaccines are used to stimulate **an immune response** in the body by creating antibodies **or** activated T lymphocytes capable of controlling the organism. **The result is protection against disease**; the duration depends on the particular vaccine. (emphasis added)"

Therefore, for the use of a vaccine to be enabled, it is fully sufficient to stimulate an immune response which can either be the generation of antibodies or activated T lymphocytes, both requirements do not need to be satisfied. The Examiner's arbitrary requirement of requiring both humoral (antibody-mediated) and cellular (T lymphocyte) responses is neither scientifically justified nor founded in the law. To fulfil the requirements of 35 U.S.C. § 112, first paragraph, it is fully sufficent that the vaccines according to the invention provide an immune response. This is extensively exemplified in Examples 2 and 3, page 21, and Tables 9 and 10 of the specification.

Likewise, the Examiner's arbitrary requirement for an adjuvant to be present in the vaccine is neither scientifically justified nor founded in the law as discussed *infra*. Appellants successfully sell Insol® Dermatophyton and Insol® Trichophyton, wherein the dermatophytes consist of the strains as claimed in claim 1 and 2 presented for review (package inserts presented in Exhibits D and E, respectively). Both vaccines do not require adjuvants due to the superior properties of the vaccine strains contained therein. Thus, it is again respectfully submitted that the subject matter claimed fully complies with the requirements set forth in 35 U.S.C. § 112, first paragraph.

In many of these allegations, the Examiner seems to be attempting to shift the burden to the appellants to affirmatively prove that appellants are entitled to a patent, when it is the Examiner's burden to prove that appellants are not entitled to a patent with rejections that are supported by evidence and a rational basis. This the Examiner has not done.

Appellants contend that the legal standard is whether a claim is understandable to one of ordinary skill in the art and that it defines subject matter that appellants regard as the invention. Federal Circuit cases have made clear that claim language must not be analyzed in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings in the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *In re Marosi*, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 221 U.S.P.Q. 1 (Fed.Cir.1983); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed.Cir.1983).

In conclusion, appellants have shown by description and examples how to produce the vaccines according to the invention, and also how to use the vaccines for prophylaxis and therapy in numerous animal species. Accordingly, appellants have shown how to make and use both vaccines within the scope of the claims.

Accordingly, appellants submit that, based on the arguments above, claims 1 and 2, comply with 35 U.S.C. § 112, first paragraph, as well as with all other statutory requirements of the U.S. Patent Law. An applicant who complies with the statutory requirements is entitled to a patent. *In re Rouffet*, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998); *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992); *In re Grabiak*, 226 U.S.P.Q. 870, 873 (Fed. Cir. 1985); *In re Rinehart*, 189 U.S.P.Q. 143, 147 (C.C.P.A. 1976).

Consequently, appellants respectfully maintain that the Examiner's rejections of pending claims 1 and 2 were improper, and request that the Board reverse all of the appealed rejections and direct the Examiner to issue a Notice of Allowance for all of the pending claims.

APPENDIX

The following claims 1 and 2 are on appeal.

1. A dermatomycosis vaccine comprising inactivated dermatophytes, wherein the inactivated dermatophytes consist of: *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277), *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279), *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278), *Trichophyton equinum* Strain No. VKPGF-929/381 (accession No. DSM 7276), *Microsporum canis* Strain No. VKPGF-928/1393 (accession No. DSM 7281), *Microsporum canis var. obesum* Strain No. VKPGF-727/1311 (accession No. DSM 7280), *Microsporum canis var. distortum* Strain No. VKPGF-728/120 (accession No. DSM 7275), and *Microsporum gypseum* Strain No. VKPGF-729/59 (accession No. DSM 7274).

2. A dermatomycosis vaccine comprising inactivated dermatophytes, wherein the inactivated dermatophytes consist of: *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277), *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279), and *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278).

Certificate of Mailing Under 37 C.F.R. § 1.8(a)
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on August 15, 2003.

Susan K. Pocchiari

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August 15, 2003

Dated

Respectfully submitted,

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THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LEE R. BECK and RALPH J. STOLLE

Appeal No. 94-3222
Application 07/815,630[1]

HEARING: July 16, 1998

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[1] Application for patent filed December 30, 1991. According to applicants, this application is a continuation of Application 07/548,419, filed July 5, 1990, now abandoned; which is (1) a continuation-in-part of Application 07/431,639, filed November 6, 1989, now U.S. 5,130,128, issued July 14, 1992; and (2) a continuation-in-part of Application 07/177,223, filed April 4, 1988, now U.S. 4,956,349, issued September 11, 1990. Application 07/431,639 is a continuation-in-part of Application 07/161,039, filed February 26, 1988, now U.S. 4,879,110, issued November 7, 1989. Both Applications 07/161,039 and 07/177,223 are continuations-in-part of Application 07/001,848, filed January 9, 1987, now U.S. 4,897,265, issued January 30, 1990; which is a divisional of Application 06/546,162, filed October 27, 1983, now U.S. 4,636,384, issued October 23, 1990; which is a continuation-in-part of Application 06/384,625, filed June 3, 1982, now abandoned. U.S. 4,636,384 was reissued as U.S. Re. 33,403 on October 23, 1990.

Before WINTERS, WILLIAM F. SMITH, and GRON, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

This is an appeal under 35 U.S.C. § 134 from an examiner's final rejection of Claims 2 and 6-9.

On consideration of the record of this case in its entirety, it is hereby ORDERED that

the examiner's final rejections in this case are VACATED, and that

this application is REMANDED to the examiner for further action consistent with the following opinion.

1. Introduction

Claims 1-9 are pending in this application. In accordance with 37 CFR § 1.142(b), Claims 1 and 3-5 have been withdrawn from further consideration by the examiner as directed to non-elected subject matter under a restriction requirement. Claims 2 and 6-9 stand rejected as unpatentable under 35 U.S.C. § 101 purportedly as drawn to subject matter without practical utility and under

35 U.S.C. § 112, first paragraph, as supported by a specification which purportedly would not have enabled persons skilled in the art to use the full scope of products and methods claimed for the utility indicated.

According to appellants, Claims 2 and 6-9 stand or fall together (Brief on Appeal, p. 4). Claims 2 and 6 represent the subject matter claimed and read:

> 2. A food product comprising a composition wherein said composition comprises a non-antibody fraction of milk and wherein said non-antibody fraction of milk ameliorates, in a subject with an allergy to an allergen, the symptoms of said allergy of said subject to said allergen when said fraction is ingested by said subject and wherein said fraction is produced by the process comprising:
>
> (a) administering said allergy to a milk-producing animal;
>
> (b) collecting the milk from said animal of part (a);
>
> (c) filtering the milk of part (b) through a filter which excludes molecules of greater than 100,000 daltons; and
>
> (d) collecting the effluent from the filtration of part (c) wherein said effluent contains said fraction.
>
> 6. A method for desensitizing a subject to an allergen wherein said method comprises orally administering to said subject a food product, in an amount and for a time sufficient to produce an amelioration in said subject of

> symptoms of allergy to said allergen, wherein said food product comprises a non-antibody fraction of milk from a milk-producing animal that has been immunized with said allergen.

2. Discussion

It should have been apparent from the questions this panel of the Board asked counsel at Oral Hearing on July 16, 1998, that we should not rule on the merits of this appeal because, as a matter of law, it would be incorrect to do so. Accordingly, we vacate the examiner's decision finally rejecting the subject matter on appeal under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, for reasons which follow.

We have searched the record of this case and do not find any indication that the metes and bounds of the subject matter claimed have been established. Where, as here, the issues presented for our review concern the practical utility of the full scope of the subject matter claimed and the specification's capacity to enable one skilled in the art to make and use the full scope of the subject matter claimed, claim interpretation is a necessary prerequisite to resolution of the merits of the issues presented. See In re Steele, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962)(When an analysis

of the claims leaves the reviewing body in a quandary as to what they cover, the examiner and the Board may not rely on speculation as to the meaning of the claims in support of a rejection.) In re Moore, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971) instructs at 1235, 169 USPQ at 238 [footnotes omitted]:

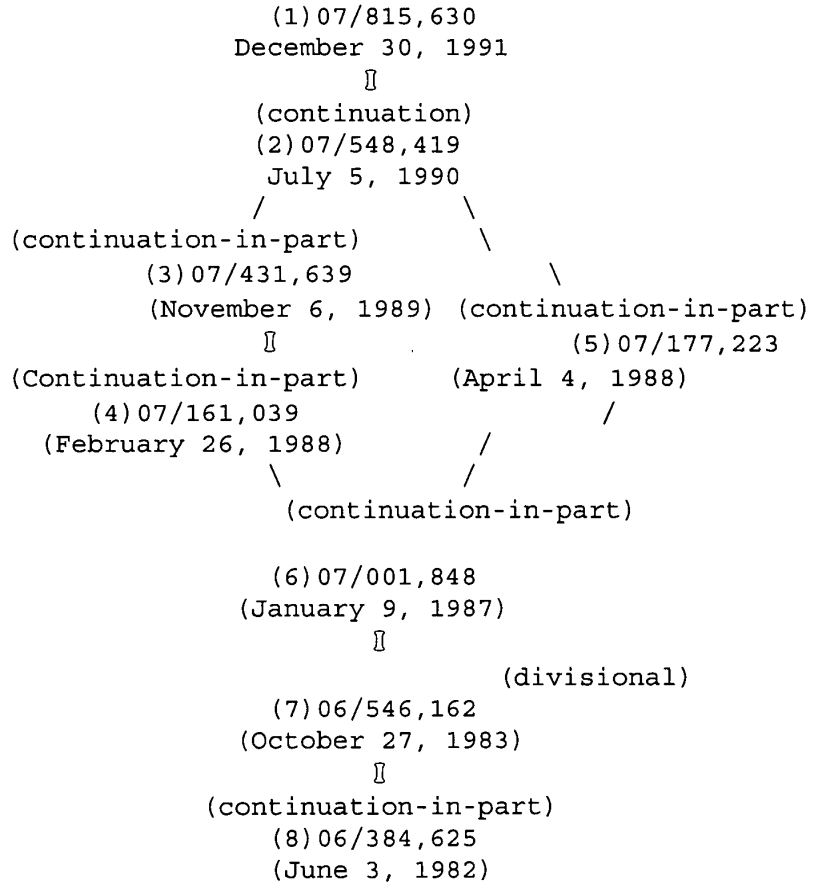
> [The] . . . first inquiry therefore is merely to determine whether the claims do . . . set out and circumscribe a particular area with a reasonable degree of precision and particularity. It is here where the definiteness of the language employed must be analyzed--not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.
>
> Once having determined that the subject matter defined by the claims is particular and definite, the analysis then turns to the first paragraph of section 112 to determine whether the scope of protection sought is supported and justified by the specification disclosure.

For example, the examiner appears not to have interpreted the term "allergen" in Claims 2 and 6, the phrases "allergy to an allergen" in Claim 2 and "allergy to said allergen" in Claim 6, the phrases "ameliorates . . . the symptoms of said allergy" in Claim 2 and "an amelioration . . . of symptoms of allergy" in Claim 6, the term "non-antibody fraction" in Claims 2 and 6, the phrase "a non-antibody fraction of milk from a milk-producing animal that has been immunized with said

allergen" in Claim 6 (emphasis added), and the phrase "excludes molecules of greater than 100,000 daltons" in Claim 2. We will refrain from considering the patentability of the claimed subject matter under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, until the examiner has first interpreted the meaning and breadth of the aforementioned terms and phrases in light of the description of the claimed subject matter in the specification and the teachings of the prior art. Id. at 1235, 169 USPQ at 238.

Moreover, we do not understand how it is possible for the examiner of this application to consider the meaning and breadth of the terms and phrases in appellants' claims in light of the prior art or to determine whether this specification would have enabled persons skilled in the art at the pertinent time to make and use the full scope of invention claimed without having first determined the effective filing date of the subject matter claimed. Unless and until the effective filing date of the subject matter presently claimed is established, what is and what is not prior art as to the subject matter presently claimed can be no more than speculative.

For example, applicants claim the benefit of priority under 35 U.S.C. § 120 through two lineages (Spec., p. 1, first para.):



With those two lines in mind, we list the following information:

(1) Application 07/815,630 for "IMMUNE SUPPRESSIVE PRODUCT," was filed December 30, 1991, in the names of Beck and Stolle.

(2) Application 07/548,419 was filed July 5, 1990, also in the names of Beck and Stolle and is said to be the parent of continuation Application 07/815,630 (this application);

(3) Application 07/431,639 for "USE OF HONEY AS VACCINE" was filed November 6, 1989, in the sole name of Stolle and issued July 14, 1992, as U.S. 5,130,128;

(4) Application 07/161,039 for "ANTIHYPERTENSIVE HYPERIMMUNE MILK, PRODUCTION, COMPOSITION, AND USE" was filed February 26, 1988, in the names of Beck and Stolle and issued November 7, 1989, as U.S. 4,879,110;

(5) Application 07/177,223 for "ANTI-INFLAMMATORY FACTOR, METHOD OF ISOLATION, AND USE" was filed April 4, 1988, in the sole name of Beck and issued September 11, 1990, as U.S. 4,956,349;

(6) Application 07/001,848 for "METHOD FOR TREATING DISORDERS OF THE VASCULAR AND PULMONARY SYSTEMS" was filed January 9, 1987, in the names of Stolle and Beck and issued January 30, 1990, as U.S. 4,897,265;

(7) Application 07/546,162 for "METHOD FOR TREATING DISORDERS OF THE VASCULAR AND PULMONARY SYSTEMS" was filed October 27, 1983, in the names of Stolle and Beck and issued January 13, 1987, as U.S. 4,636,384; and

(8) Application 07/384,625, now abandoned, was filed June 3, 1982, in the names of Stolle and Beck.

We note from the above listing that while the subject matter appellants claim appears to be entitled to the July 5, 1990, filing date of (2) Application 07/548,419 filed in the names of Beck and Stolle as a file-wrapper continuation of this application, it is not at all apparent that the full scope of the subject matter presently claimed is entitled either to the November 6, 1989, filing date of (3) Application 07/431,639 for "USE OF HONEY AS VACCINE" filed in the sole name of Stolle or the April 4, 1988, filing date or (5) Application 07/177,223 for "ANTI-INFLAMMATORY FACTOR, METHOD OF ISOLATION, AND USE" filed in the sole name of Beck. In fact, this record is noticeably devoid of any indication that the effective filing date of the subject matter claimed has been determined. Accordingly, it is our view that claim interpretation in light of the prior art cannot have been adequately done without first determining the merits of

applicants' claims under 35 U.S.C. § 120 so as to enable one to establish what constitutes the prior art under 35 U.S.C. § 102.

Moreover, while compliance with the requirements of 35 U.S.C. § 112, first paragraph, is normally determined as of the filing date of the pending application, the examiner, when faced with an intervening reference, may be required to focus on the filing date of a prior application as the result of the applicants' claims for priority under 35 U.S.C. § 120. United States Steel Corp. v. Phillips Petroleum Co., 865 F.2d 1247, 1251, 9 USPQ2d 1461, 1464 (Fed. Cir. 1989). We appear to have just such a case before us.

On their face, Stolle, U.S. 5,130,128, filed November 6, 1989, and Beck, U.S. 4,956,349, filed April 4, 1988, appear to be prior art under 35 U.S.C. § 102(e) whether or not they are commonly assigned with this application filed in the names of Beck and Stolle. See In re Bartfeld, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991). Moreover, Stolle and Beck, U.S. 4,636,384 and U.S. 4,732,757 may be prior art under 35 U.S.C. § 102(b). Accordingly, faced with what prima facie appears at least in part to be prior art of record and applicants' claims for priority under 35 U.S.C. § 120 in this case, the examiner

should determine the effective filing date of the subject matter here claimed before ruling on patentability under either 35 U.S.C. § 112, first paragraph, § 101, § 102, or § 103. It is as of the effective filing date that compliance with 35 U.S.C. §§ 112, first paragraph, and 101 and prior art availability must be determined.

Only after determining the effective filing date of the subject matter claimed may the examiner (1) determine whether appellants' claims satisfy 35 U.S.C. § 112, second paragraph, in light of applicants' disclosure and the prior art, (2) consider whether the subject matter claimed is patentable under 35 U.S.C. § 101 or whether applicants' disclosure would have enabled one skilled in the art to make and use the full scope of the claimed subject matter as required by 35 U.S.C. § 112, first paragraph, (3) determine patentability under 35 U.S.C. §§ 102 and 103 in view of the prior art (compare Chester v. Miller, 906 F.2d 1574, 1576, 15 USPQ2d 1333, 1336 (Fed. Cir. 1990), citing In re Gosteli, 872 F.2d 1008, 1010-1011, 10 USPQ2d 1614, 1616 (Fed. Cir. 1989)), and (4) determine whether the subject matter claimed in this case is unpatentable for obviousness-type

double-patenting of subject matter claimed in any one or more of the U.S. patents which have issued from applications for which

priority under 35 U.S.C. § 120 here is claimed.[2]

We will allow the examiner of this case to determine in the first instance the effective filing date of the subject matter claimed, the scope and content of the pertinent prior art, compliance with the requirements of the second paragraph of Section 112, compliance with Section 101 and the first paragraph of Section 112, and patentability of the claimed subject matter under 35 U.S.C. § 102, under 35 U.S.C. § 103, and over subject matter claimed in commonly assigned patents absent the filing of effective terminal disclaimers. For this panel to review the merits of the examiner's decision rejecting the claims on appeal under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, at this time without those preliminary determinations having been made by an examiner is

---

[2] The examiner may wish to consider obviousness-type double-patenting issues. However, take note that if questions of obviousness-type double patenting of subject matter claimed in issued patents come to light, the examiner may want to consider whether adhering to unpatentability determinations under 35 U.S.C. § 101 or 112, first paragraph, for lack of utility is consistent with the presumption of validity of the patented subject matter.

inconsistent with our review function. See 35 U.S.C. § 7 ("The Board . . . shall . . . review adverse decisions of examiners . . . .") Accordingly, we vacate the examiner's final rejections and remand the case to the examining corps for action consistent with this opinion.

This application, by virtue of its "special" status, requires an immediate action, M.P.E.P. § 708.01(d). It is important that the Board be informed promptly of any action affecting the appeal in this case.

VACATED and REMANDED

SHERMAN D. WINTERS Administrative Patent Judge	)
WILLIAM F. SMITH Administrative Patent Judge	) BOARD OF PATENT APPEALS AND INTERFERENCES
TEDDY S. GRON	)

Administrative Patent Judge)

[redacted]

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte YUPIN CHAROENVIT, STEPHEN L. HOFFMAN,
RICHARD L. BEAUDOIN, DECEASED, BY BARBARA A. BEAUDOIN

Appeal No. 1999-1413
Application No. 08/176,024

ON BRIEF

Before SCHEINER, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

[redacted]

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 7, 11, and 12, which are all of the claims pending in the application.

Claims 1, 4, and 11 are representative and read as follows:

1. A formulation protective against Plasmodium vivax for a time commensurate with the time monoclonal antibody Navy Vivax Sporozoite 3 (HB10615) remains at pharmacologically active levels in a subject's blood stream, comprising a pharmaceutical amount sufficient to provide passive immunization of Navy Vivax Sporozoite 3 (HB10615) in a pharmaceutically suitable injectable solution.

4. A method of providing protection from Plasmodium vivax induced malaria for subjects experiencing exposure to infected mosquitoes, for a time commensurate with the time monoclonal antibody Navy Vivax Sporozoite 3 (HB 10615) remains at pharmacologically active levels in a subject's blood stream, that comprises introducing and circulating the antibody Navy Vivax Sporozoite 3 (HB 10615) in the subject's blood stream.

11. A humanized antibody capable of providing passive protection against Plasmodium vivax wherein said antibody has a variable region comprising the hyper variable regions of the heavy and light chains of monoclonal antibody Navy Sporozoite 3 (HB10615) and human antibody framework regions.

The examiner relies on the following references:

McCutchan et al (McCutchan 1) 4,694,944 Sept. 15, 1987

McCutchan, T.F. et al (McCutchan 2). "Sequence of the Immunodominant Epitope for the Surface Protein Sporozoites of Plasmodium vivax," Science, Vol. 23, pp. 1381-1383 (1985)

Harlow et al. (Harlow), Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory pp. 287 (1988)

Charoenvit, Y. et al. (Charoenvit), "Inability of Malaria Vaccine to Induce Antibodies to a Protective Epitope Within its Sequence," Science, Vol. 251, pp. 668-671 (1991)

Harris et al. (Harris), "Therapeutic Antibodies - The Coming of Age," Tibtech, Vol. 11, pp. 42-44 (1993)

Mitchell, G. H., (Mitchell), "An Update on Candidate Malaria Vaccines," Parasitology, Vol. 98, New York, pp. S29-S46 (1989)

Grounds of Rejection

1. Claims 1-3 stand rejected under 35 U.S.C. §103. As evidence of obviousness, the examiner cites McCutchan (1 and 2) and Harlow.

2. Claims 1-7, 11 and 12 stand rejected under 35 U.S.C. §112, first paragraph. As evidence of nonenablement, the examiner cites Charoenvit, Harris, and Mitchell.

We reverse both rejections.

DISCUSSION

Procedural Matters

In this case, an Appeal Brief with four attached 1.132 declarations was filed concurrent with a proposed amendment, on March 1, 1996. After several interviews and written communications, amended claims were entered by the Examiner, the effect of amendment entry on the rejections of record was communicated to the appellant on August 21, 1996, and a Substitute Brief was filed September 20, 1996, containing arguments directed to the amended claims. The Substitute Brief also refers to the

declarations by Drs. Steven L. Hoffman (1st and 2nd declarations), Yupin Charoenvit, and Thomas F. McCutchan, which were attached to the original Brief.

In the Examiner's Answer, four rejections under 35 U.S.C. § 103 were withdrawn. No new grounds of rejection were made, and no Reply Brief was filed.

Background

Plasmodium vivax is one of the four species of parasite causing malaria in humans (specification, page 1). Despite major efforts over at least 20 years, a commercially viable malaria vaccine has not been achieved (page 2 of the December 28, 1993 amendment to the specification). The present invention involves a monoclonal antibody, here designated NVS3. The monoclonal antibody has been described in the prior art (specification, page 2). This antibody binds to an epitope within a repeated nine amino acid sequence of the circumsporozoite protein of P. vivax (specification, page 8). Prior to the invention, recombinant proteins comprising the P. vivax repeated amino acid sequence failed to induce a significant protective effect in Saimiri monkeys in active immunization experiments (specification, pages 3-4). An object of this invention is to provide passive protection against P. vivax by administering the antibody to a subject, where the antibodies

bind to P. vivax sporozoites in the circulation of the host and render the sporozoites noninfectious thereby preventing malarial disease (specification, pages 4 and 7-8).

Enablement

Claims 1-7, 11 and 12 stand rejected under 35 U.S.C. §112, first paragraph. As evidence of nonenablement, the examiner cites Charoenvit, Harris, and Mitchell.

Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." In re Wands, 858 F.2d 73, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie

case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F2d 162, 165, 192 USPQ 29, 32 (CCPA 1976). The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement.

Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In the present case, the examiner cites the state of the art and the lack of working examples involving humans as the factors leading to a conclusion of non-enablement. Specifically, the examiner argues (Answer, page 6):

> The state of the art to which the invention pertains is such that as of this date passive immunization has not been used to prevent malaria in humans and that there are no vaccines for active or passive immunization that are accepted as being effective for prevention of P. vivax malaria. Charoenvit et al. (Science 251) states that it has never been definitively established in humans that circulating antibodies to the sporozoite of Plasmodium can prevent infection. Furthermore, Harris et al. establishes the use of monoclonal antibodies for in vivo human therapy is art-recognized to be highly experimental and unpredictable to those of skill in the art. The record contains no working examples relating to the use of the NVS3 antibody for treatment of P. vivax malaria in humans....
>
> The invention has been exemplified using the monkey model. However, the evidence obtained using the monkey model is not sufficient to allow one of ordinary skill in the art to predict the ability to practice the claimed invention for treatment of humans given that the monkey model used to exemplify the claimed invention is not an art-accepted model which is recognized as having a clear correlation with human efficacy for the evaluation of agents for passive immunotherapy of malaria.

On the other hand, the appellants argue that proof of efficacy in humans is not required, and that the monkey animal model tests disclosed in the specification are accepted by experts in the field. Substitute Brief, pages 13-15.

The specification provides a working example demonstrating efficacy of the claimed formulation in a nonhuman primate, the Saimiri monkey. Example 3, pages 13-15. In addition, the Hoffman Declaration of record provides an expert opinion that "most experts in the field consider this monkey model to be the most reliable system for predicting what will occur in humans." Hoffman Declaration, page 6. The Hoffman Declaration also cites long-held knowledge in the art of passive immunotherapy for acute malaria in human children. Hoffman Declaration, pages 4-5.

[redacted]

Although the examiner considered several scientifically conservative statements regarding the acceptability of the animal model of record, such as, "this monkey model system has not been validated" (Hoffman declaration, page 6), and "[w]ith the exception of the work carried out in man, the validity of all the experimental systems is open to challenge" (Mitchell, page 2), we do not find that the examiner has reviewed the evidence of enablement provided by appellants as a whole.

The cases of In re Fouche, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971) and In re Brana, 51 F.3d 1560, 1563, 34 USPQ2d 1436, 1439 (Fed. Cir. 1995), recognize that 35 U.S.C. §101 rejections for utility present similar issues as 35 U.S.C. §112 rejections for nonenablement. Thus, it is appropriate to consider relevant utility case law to the present enablement issue.

In Brana, the Federal Circuit stated, "Our court's predecessor has determined that proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility." In re Brana, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995); In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961). In addition, "...pharmacological testing of animals is a screening procedure for testing new drugs for practical utility." Cross v. Iizuka, 753 F.2d 1040, 1051, 224 USPQ 739, 747 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1324, 1327, 206 USPQ 885, 890 (CCPA 1980).

It is appellants' position that successful in vivo testing for a particular pharmacological activity in an art accepted model (monkeys) establishes a significant probability that in vivo testing for this particular pharmacological activity will be successful in humans. On the facts before us, we agree.

Appellants submit that they have provided evidence of efficacy of the claimed formulation protective against Plasmodium vivax in the most reliable and standard animal model accepted by experts in the field for predicting the likelihood of success of the claimed invention in humans. Substitute Brief, page 13.

Based upon the relevant evidence as a whole, we find there to be a reasonable correlation between the disclosed in vivo utility and an in vivo activity in humans, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. Compare Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); Nelson v. Bowler, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980). Therefore, we will not sustain the rejection of the claims for lack of enablement.

Obviousness

Claims 1-3 stand rejected under 35 U.S.C. §103. As evidence of obviousness, the examiner cites McCutchan (1 and 2) and Harlow.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). A reference is considered in its entirety for what it fairly suggests to one skilled in the art. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

According to the examiner, McCutchan 1 and 2 describe monoclonal antibodies which are specific for epitopes of a peptide which corresponds to a region of the P. Vivax CS (circumsporozite) protein. The specification, page 2, states that the monoclonal antibody disclosed by McCutchan et al (Science 230) and McCutchan et al (U.S. Patent No. 4,693,994) is the monoclonal antibody of the instant invention which is designated NVS3. Answer, page 5. The examiner acknowledges that the McCutchan references do not teach a composition comprising a pharmaceutical amount of a monoclonal antibody NVS3 in a pharmaceutically acceptable carrier. Id.

Harlow is cited by the examiner as establishing that it was well known in the art at the time of the invention to produce solutions of monoclonal antibodies in phosphate

buffered saline (PBS) which is considered to be a pharmaceutically acceptable diluent for storage of antibodies.

The examiner summarizes (Answer, pages 5-6),

> It would have been obvious for one of ordinary skill in the art to produce solutions consisting of NVS3 monoclonal antibody as taught by McCutchan et al references. One of ordinary skill in the art would have been motivated to produce such compositions in order to form stable storage compositions, or working solutions for us in assays, etc. The antibody concentrations in such compositions would have been those which would be considered to be pharmaceutical amounts, and solutions comprising the NVS3 antibody PBS would be considered to be pharmaceutically injectable solutions given that the buffer PBS is a pharmaceutically acceptable diluent. Even though the appellants characterize the claimed formulations as being for use in passive protection against *P.vivax*, the claims read on the ingredients *per se*, which in the case of the instant claims are NVS3 antibody in a pharmaceutically acceptable carrier.

Appellants argue in response to this rejection that, at best the examiner has argued that it would be obvious to try using the NVS3 monoclonal antibody for passive immunization and that it would have some protective activity. Substitute Brief, page 24. Appellants argue the examiner has failed to provide evidence to support a reasonable expectation of the success of passive immunization using the monoclonal antibody, as claimed. Id. Furthermore, appellants argue that Harlow teaches away from the invention by recommending addition of sodium azide, a poison, as a preservative in monoclonal antibody solutions. Substitute Brief, page 32.

We agree with appellants that the examiner has failed to establish a prima facie case of obviousness on the record before us. McCutchan teaches the claimed monoclonal

antibody in the context of an analytical tool. Harlow, the secondary reference, states that when preparing a PBS solution of monoclonal antibodies in the laboratory, "[i]f there is no reason to avoid the use of sodium azide, add to 0.02%". Harlow, page 287. In our view, neither reference, however, provides any reason for one of ordinary skill in the art to avoid the use of sodium azide in preparing a monoclonal antibody solution, such as for preparing a composition for use in vivo.

The diagnostic use of a monoclonal antibody as described by McCutchan 1 and 2, in view of Harlow, would reasonably appear to have suggested that sodium azide be used in preparing such monoclonal antibody solutions. Therefore, taking the teachings of the references in their entirety, the references as a whole would have suggested to one of ordinary skill in the art a composition comprising a monoclonal antibody, PBS and sodium azide in an antibody solution, leading to a solution which is not a pharmaceutically acceptable formulation, as claimed. Moreover, we find no evidence of record suggesting the use of, or supporting a reasonable expectation of success for the use of the monoclonal antibody for preparation of a pharmaceutical formulation for passive immunization against P. vivax. Therefore, we will not sustain the rejection of the claims for obviousness.

CONCLUSION

The rejection of claims 1-3 under 35 U.S.C. §103 in view of McCutchan (1 and 2) and Harlow is reversed.

The rejection of claims 1-7, 11 and 12 under 35 U.S.C. §112, first paragraph is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

Toni R. Scheiner Administrative Patent Judge	)
Demetra J. Mills Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Eric Grimes Administrative Patent Judge	)

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V 1. *Vibrio; vision; visual acuity.* **2.** Symbol for the element vanadium.

V̇ 1. Symbol for gas flow. **2.** Symbol for ventilation.

v L. *vena*, vein; *volt.*

vaccina (văk-sī'nă) Vaccinia.

vaccinable (văk-sĭn'ă-b'l) Capable of being successfully vaccinated.

vaccinal (văk'sĭn-ăl) Rel. to vaccine or to vaccination.

vaccinate (văk'sĭn-āt) [L. *vaccinus*, pert. to cows] To inoculate with vaccine to produce immunity against disease.

vaccination (văk"sĭ-nā'shŭn) [L. *vaccinus*, pert. to cows] **1.** Inoculation with any vaccine or toxoid to establish resistance to a specific infectious disease. SEE: *immunization.* **2.** A scar left on the skin by inoculation of a vaccine.

vaccine (văk'sēn, văk-sēn') [L. *vaccinus*, pert. to cows] A suspension of infectious agents, or some part of them, given for the purpose of establishing resistance to an infectious disease. SEE: table.

Vaccines comprise four general classes:

1. Those containing living attenuated infectious organisms, such as vaccine for poliomyelitis.
2. Those containing infectious agents killed by physical or chemical means, such as vaccines used to protect human beings against typhoid fever, rabies, and whooping cough.
3. Those containing soluble toxins of microorganisms, sometimes used as such, but generally forming toxoids, such as the one used in the prevention of diphtheria and tetanus.
4. Those containing substances extracted from infectious agents, such as capsular polysaccharides extracted from pneumococci.

FUNCTION: Vaccines are used to stimulate an immune response in the body by creating antibodies or activated T lymphocytes capable of controlling the organism. The result is protection against a disease; the duration depends on the particular vaccine. Recovery from measles or diphtheria, for example, usually provides lifelong immunity. The immune system has produced antibodies and memory cells for these pathogens so that subsequent exposure does not result in disease. A successful vaccine does the same thing, usually without risk of illness. The measles vaccine is believed to provide lifelong immunity, but the diphtheria vaccine requires periodic booster doses. More than one type of vaccine may be available for immunization against a specific infectious agent. SEE: *diphtheria; immune response; immunity; immunization; immunobiologics.*

autogenous v. Bacterial vaccine pared from lesions of the individual inoculated. SYN: *homologous v.*

bacterial v. A suspension of killed tenuated bacteria; used for injectior the body to induce development of a immunity to the same organism.

BCG v. Bacille Calmette-Guéri preparation of a dried, living cultu *Mycobacterium tuberculosis.* In with a high incidence of tuberculosis used in prophylactic vaccination c fants against tuberculosis. It is also in adults who are at high and unavoi risk of becoming infected with tuber sis. A disadvantage of use of this va is that it produces hypersensitivity berculin. As a result, the skin test fc berculin sensitivity becomes positive may persist for 5 years. There is no to distinguish a positive skin test d BCG from one caused by infection *Mycobacterium tuberculosis.*

cholera v. A vaccine prepared killed *Vibrio cholerae.* It is effectiv only a few months.

diphtheria v. SEE: *DPT v.*

DPT v. A combination of diphtheri tetanus toxoids and killed pertussi cilli that is administered intramuscu to immunize children against diphth tetanus, and pertussis.

DTaP v. A preparation of diphtl and tetanus toxoids and acellular pe sis proteins. It may be used for the fo and fifth injections in the series.

Haemophilus influenzae type b vaccine prepared from the bacterial saccharide (HbPV) or polysaccharide verted to protein (HbCV).

hepatitis B v. A vaccine prepared hepatitis B protein antigen produce genetically engineered yeast.

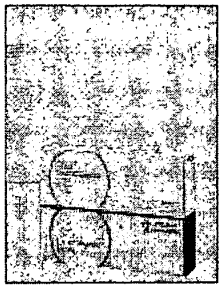
heterologous v. A vaccine derived an organism different from the orga against which the vaccine is used.

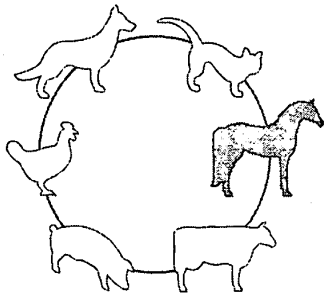
homologous v. Autogenous v.

human diploid cell rabies v. A HDCV. An inactivated virus vaccine pared from fixed rabies virus grown ir man diploid cell tissue culture.

inactivated poliovirus v. An inject vaccine made from three types of in vated polioviruses. Previously used n poliomyelitis vaccine. SYN: *Salk v.*

influenza virus v. A polyvalent vac containing inactivated antigenic vari of the influenza virus (types A and ther individually or combined) for us areas expected to have epidemics. Its





Insol® Dermatophyton

Inactivated dermatophytosis vaccine

Dermatophytosis is the contagious superficial infection of the skin caused by dermatophytes (ringworm or tinea) and it is the most common skin disease in horses. The spores can survive for years.
Insol(r) Dermatophyton contains highly immunogenic strains of fungus. Based on a special manufacturing process the inactivated microconidia stimulate cell-mediated immune response in particular.
Insol(r) Dermatophyton contains no adjuvants, adsorbents, additives or excipients.

Indications

Active immunisation of horses, dogs, cats, rabbits and guinea pigs against dermatophytosis caused by trichophyton verrucosum, trichophyton mentagrophytes, trichophyton sarkisovii, trichophyton equinum, microsporum canis, microsporum gypseum and for the treatment of animals infected by dermatophytosis caused by these fungal species.

Features

- First vaccine against dermatophytosis in horses
- Covers all relevant strains
- For prophylaxis and therapy
- Easy application/handling

Benefits

- Comfortable way to combat dermatophytosis
- Safe for humans, safe for animals
- Vaccination during incubation possible
- 12 months protection appropriate for long term disease control

Presentation and mode of administration

Available in 5 x 2 ml glass vials for injection
For both prophylactic and therapeutic use 2 intramuscular injections 14 days apart on alternate sides of the body:

- horse ≤400 kg b.w.: 0.3 ml;
  400 - 600 kg b.w.: 0.5 ml; >600 kg b.w.: 0.7 ml
- dogs ≤10 kg b.w.: 0.3 ml; 10 - 40 kg b.w.: 0.5 ml;
  >40 kg b.w.: 1.0 ml
- cats <1 kg b.w.: 0.5 ml; >1 kg b.w.: 1.0 ml
- rabbits <3 kg b.w.: 0.5 ml; >3 kg b.w.: 1.0 ml
- guinea pigs: per 100 g b.w.: 0.1 ml

repeat vaccination at yearly intervals.

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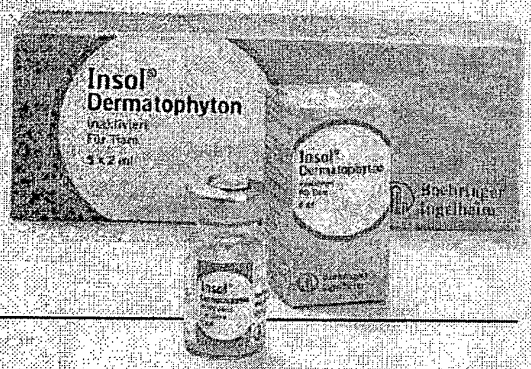
Insol® Dermatophyton

Suspension

Für Tiere

Zusammenfassung der Produkteigenschaften



Bei jeder Injektion sollte die Körperseite gewechselt werden.
Zur Aufrechterhaltung des Impfschutzes sollten Wiederholungsbehandlungen nach prophylaktischer bzw. therapeutischer Anwendung in Form von zwei Impfungen im Abstand von 14 Tagen alle 10 bis 12 Monate erfolgen.

5.8 Überdosierung
Eine Überdosierung kann zu einer Verstärkung der aufgeführten Nebenwirkungen führen.

5.9 Besondere Warnhinweise für die Zieltierarten
keine

5.10 Wartezeit
Essbare Gewebe vom Pferd: 3 Tage

5.11 Besondere Vorsichtsmaßnahmen für Personen bei der Anwendung des Produktes
keine
Im Falle eines versehentlichen Verschüttens des Impfstoffes auf die Haut ist diese mit Wasser abzuwaschen.
Versehentliche Selbstinjektion kann zu vorübergehenden Schwellungen an der Injektionsstelle führen. In Fällen schwerer Nebenwirkungen nach versehentlicher Selbstinjektion mit dem Impfstoff sollte ein Arzt aufgesucht werden.

6. Pharmazeutische Daten

6.1 Unverträglichkeiten
Bezüglich möglicher Inkompatibilitäten wurden keine Studien durchgeführt.
Der Impfstoff darf nicht mit anderen Impfstoffen gemischt werden.

6.2 Haltbarkeit
Im ungeöffneten Behältnis:
36 Monate bei einer Lagerung zwischen +2°C bis +8°C
Im geöffneten Behältnis:
14 Tage bei einer Lagerung zwischen +2°C bis +8°C, sofern die Entnahmen ordnungsgemäß erfolgen.

6.3 Hinweise zur Aufbewahrung
Der Impfstoff ist zwischen +2°C und +8°C zu lagern!
Nicht einfrieren! Vor Licht schützen!
Impfstoff für Kinder unzugänglich aufbewahren!

6.4 Behältnis
2 ml-, 5 ml-, oder 10 ml-Glasflaschen der Glasart I, verschlossen mit Brombutyl-Gummistopfen und Aluminiumbördelkappen

6.5 Zulassungsinhaber
Boehringer Ingelheim
Vetmedica GmbH
55216 Ingelheim
Hersteller
Serumwerk Memsen
27318 Hoyerhagen

6.6 Besondere Hinweise für die Beseitigung von unbrauchbarem Material
Leere Behälter, nicht völlig aufgebrauchter oder nach Ablauf des Verfalldatums nicht mehr verwendbarer Impfstoff sind unschädlich zu beseitigen.

7. Weitere Informationen

Zulassungs-Nummer: 118a/96

Datum der Genehmigung dieser Zusammenfassung der Produkteigenschaften:
24. 01. 2000

Abgabestatus: Verschreibungspflichtig

Zugelassene Handelsformen:
Packung mit 2 ml
Packung mit 5 x 2 ml

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim am Rhein
Telefon 01803/660660

Boehringer Ingelheim

316/0010

1. Name

Insol® Dermatophyton

2. Zusammensetzung

1 ml der inaktivierten Vakzine enthält jeweils mind. $6{,}25 \times 10^{5,0}$ Mikrokonidien der folgenden Pilzstämme:

- Trichophyton verrucosum, Stamm Nr. 410
- Trichophyton mentagrophytes, Stamm Nr. 1032
- Trichophyton sarkisovii, Stamm Nr. 551
- Trichophyton equinum, Stamm Nr. 381
- Mikrosporum canis, Stamm Nr. 1393
- Mikrosporum canis var. distortum, Stamm Nr. 120
- Mikrosporum canis var. obesum, Stamm Nr. 1311
- Mikrosporum gypseum, Stamm Nr. 59

und maximal 0,044 mg Thiomersal in einer Glucose-Fleischextrakt-Suspension.

3. Darreichungsform

Suspension zur Injektion

4. Immunologische Eigenschaften

Die Verabreichung des Impfstoffes bewirkt die Ausbildung einer Immunität bei Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophytosen, verursacht durch Trichophyton verrucosum, Trichophyton mentagrophytes, Trichophyton sarkisovii, Trichophyton equinum, Mikrosporum canis und Mikrosporum gypseum.

Die im Impfstoff enthaltenen Stämme sind tierischen Ursprungs: Trichophyton verrucosum (Stamm Nr. 410) wurde von einem Rentier, Trichophyton mentagrophytes (Stamm Nr. 1032) von einem Pferd, Trichophyton sarkisovii (Stamm Nr. 551) von einem Kamel, Trichophyton equinum (Stamm Nr. 381) von einem Pferd, Mikrosporum canis (Stamm Nr. 1393) von einer Katze, Mikrosporum canis var. distortum (Stamm Nr. 120) von einem Schwarzen Panther, Mikrosporum canis var. obesum (Stamm Nr. 1311) von einem Tiger und Mikrosporum gypseum (Stamm Nr. 59) von einem Pferd isoliert.

Die erzeugte Immunität ist hauptsächlich eine zell-vermittelte Immunantwort und hält in der Regel 10 bis 12 Monate an.

5. Klinische Daten

5.0 Zielttierarten

Pferde, Hunde, Katzen, Kaninchen und Meerschweinchen.

5.1 Anwendungsgebiete

Zur aktiven Immunisierung von Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophytosen, verursacht durch Trichophyton verrucosum, Trichophyton mentagrophytes, Trichophyton sarkisovii, Trichophyton equinum, Mikrosporum canis und Mikrosporum gypseum zum Zwecke der Reduktion des Risikos einer klinischen Infektion durch diese Pilzarten, sowie als therapeutische Maßnahme zur Beschleunigung der Abheilung der klinisch sichtbaren Hautveränderungen bei Tieren, die an einer durch diese Pilzarten verursachten Dermatophytose erkrankt sind.

5.2 Gegenanzeigen

Tiere mit Fieber und/oder mit dermatophytosenunabhängigen Symptomen einer infektiösen Erkrankung, sowie Tiere, die unter Kortikoid-Wirkung stehen, sollten nicht geimpft werden.

Jungtiere entsprechend den folgenden Angaben sind von einer Impfung auszuschließen:

Pferde unter 5 Monaten
Hunde unter 6 Wochen
Katzen unter 1 Monat
Kaninchen unter 6 Wochen
Meerschweinchen unter 150 g

Nicht geimpft werden dürfen gestresste Tiere, z.B. Pferde im Auktionsstress.

Insol® Dermatophyton
Zusammenfassung der Produkteigenschaften

5.3 Nebenwirkungen

Nach der Injektion können, besonders bei Pferden, bis zu hühnereigroße Schwellungen an der Injektionsstelle auftreten, die innerhalb von 3 bis 5 Tagen ohne weitere therapeutische Maßnahmen abheilen. In Einzelfällen wurden schmerzhafte, bis zu handflächengroße Schwellungen an der Injektionsstelle in Verbindung mit gestörtem Allgemeinbefinden (z.B. Fieber, Inappetenz, Apathie) beobachtet, die innerhalb von 8 bis 10 Tagen abgeklungen waren. In solchen Fällen ist eine symptomatische Behandlung zu empfehlen, wobei von lokal reizenden Mitteln abgesehen werden sollte.

5.4 Besondere Hinweise für den Gebrauch

Bei Tieren, die sich zum Zeitpunkt der Impfung im Inkubationsstadium befinden, kann es trotz Impfung zum Ausbruch der Erkrankung kommen. Die Hautveränderungen heilen jedoch innerhalb von 2 bis 4 Wochen nach 2. Injektion ab.

Da sich auch im Haarkleid der Tiere Dermatophytose-Erreger befinden können und diese durch die Impfung nicht erreicht werden, ist das Zoonosen-Risiko durch die Impfung zwar deutlich vermindert, aber nicht vollständig ausgeschlossen. Aus diesem Grunde, sowie auch zur Senkung des Infektionsdruckes, ist bei langhaarigen Tieren das Scheren der Haare zu empfehlen. Aus dem gleichen Grunde wird empfohlen, auch solche Tiere zu impfen, die in direktem oder indirektem Kontakt zu infizierten Tieren stehen. Zur Reduktion des allgemeinen Infektionsdruckes sollten außerdem Reinigungs- und Desinfektionsmaßnahmen der Umgebung sowie der Gebrauchsgegenstände (z.B. Putzzeug) durchgeführt werden.

Erfahrungen aus der Praxis haben gezeigt, dass insbesondere in Edelkatzenbeständen, in denen ein erhöhter Infektionsdruck zu erwarten ist, eine verminderte Wirksamkeit auftreten kann bzw. eine Rezidivneigung beobachtet werden kann.

5.5 Anwendung während Trächtigkeit und Laktation

Aufgrund des Manipulationsstresses stellen Impfungen zu Beginn und gegen Ende der Trächtigkeit allgemein ein Risiko dar und sollten deshalb vermieden werden.

5.6 Wechselwirkungen

Studien zu möglichen Wechselwirkungen wurden nicht durchgeführt.

Es wird jedoch empfohlen, zwischen den Impfungen, sowie innerhalb von 14 Tagen vor und nach den Impfungen keine anderen Immunisierungen vorzunehmen.

5.7 Dosierung und Art der Anwendung

Vor Gebrauch gut schütteln!

Die Impfdosis beträgt für

Pferde:
unter 400 kg KGW 0,3 ml
400–600 kg KGW 0,5 ml
über 600 kg KGW 0,7 ml

Hunde:
bis 10 kg KGW 0,3 ml
10 bis 40 kg KGW 0,5 ml
über 40 kg KGW 1,0 ml

Katzen:
bis 1,0 kg KGW 0,5 ml
über 1,0 kg KGW 1,0 ml

Kaninchen:
bis 3,0 kg KGW 0,5 ml
über 3,0 kg KGW 1,0 ml

Meerschweinchen:
pro 100 g KGW 0,1 ml

Sowohl zur Prophylaxe als auch zur Therapie sind 2 intramuskuläre Injektionen im Abstand von 14 Tagen erforderlich.

Ist bei an einer Dermatophytose erkrankten Tieren zwei Wochen nach zweiter Injektion noch keine eindeutige Verbesserung der Haut- und Haardefekte erkennbar, wird eine dritte Injektion empfohlen.

Auf eine strenge intramuskuläre Injektion ist zu achten; eine subkutane Injektion ist unbedingt zu vermeiden.

LM

Insol® Trichophyton

Boehringer Ingelheim

Inactivated trichophytosis vaccine for cattle

Aqueous suspension for intramuscular injection

Composition

1 ml of inactivated vaccine contains:
at least 17 x $10^{6.0}$ microconidia of each of the following strains of fungi:
- Trichophyton verrucosum, strain no. 410
- Trichophyton mentagrophytes, strain no. 1032
- Trichophyton sarkisovii, strain no. 551

and a maximum of 0.040 mg thimerosal
in a glucose meat extract suspension

Indications

Active immunisation of cattle from the age of 1 month onwards against trichophytosis caused by Trichophyton verrucosum, Trichophyton mentagrophytes and/or Trichophyton sarkisovii and as an aid in the treatment of cattle infected by trichophytosis caused by these fungal species.

Contraindications

None.

Undesirable effects

Slight swelling can occur at the injection site (mostly after accidental subcutaneous injection) which clears with no adverse symptoms.
In exceptional cases (ca. 0.05%) shock reactions in the form of dyspnoea, pulmonal oedema, reddish foam around the mouth and nose and heavy transpiration can occur (death can occur in ca. 0.01% of the vaccinated animals). In such cases symptomatic treatment including administration of adrenalin, glucocorticoids and antihistamines, possibly together with a dose of calcium, is indicated.

Special Precautions for use

In the case of animals which are in the incubation phase at the time of vaccination, the disease can still break out in spite of the vaccination. However, the skin lesions heal 2–4 weeks after the second injection.

Use during pregnancy and lactation

The vaccination can be carried out at any stage of pregnancy. To date no effect on milk output has been observed.

Interactions

No interaction studies have been performed.

However, it is recommended that no other immunisations be carried out between the vaccinations or within 14 days before and after the vaccinations.

Posology and method of administration

Shake well before use.

The vaccination dose is
for cattle with less than 70 kg bodyweight: 2.5 ml

for cattle with more than 70 kg bodyweight: 5.0 ml

ueous suspension for intramuscular
section.
ase follow instructions carefully.
nl of inactivated vaccine contains:
least 17 x $10^{6.0}$ microconidia of each
the following strains of fungi:
Trichophyton verrucosum,
strain no. 410
Trichophyton mentagrophytes,
strain no. 1032
Trichophyton sarkisovii,
strain no. 551
d a maximum of 0.040 mg thimerosal
a glucose meat extract suspension

Boehringer Ingelheim

LM
Insol® Trichophyton
Inactivated trichophytosis vaccine for cattle
100 ml

Withdrawal Periods:
Edible Tissue: 3 days
Milk: none

Storage:
Store at between +2°C and +8°C.
Do not freeze. Protect from light.
Once the bottle has been opened, the vaccine may be used for up to 14 days if extracted properly and stored in a cool place.

FOR ANIMAL TREATMENT ONLY
KEEP OUT OF REACH OF CHILDREN

Authorisation No: AR8/003/01

Boehringer Ingelheim Limited.
Ellesfield Avenue, Bracknell
Berks., RG12 8YS

9038
V 10153/IE/1

Batch No.:

Expiry Date:

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Inactivated trichophytosis vaccine for cattle
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Ellesfield Avenue, Bracknell
Berks., RG12 8YS

9038
V 10153/IE/1

Batch No.:

Expiry Date:

Both for prophylaxis and for therapy 2 intramuscular injections with a 14-day interval are required. The injections should be given on alternate sides of the body. To maintain the vaccine protection after prophylactic or therapeutic administration, repeat vaccinations should be carried out at yearly intervals.

Subcutaneous injection is to be avoided

Overdose
Can lead to slight local intolerance reactions.

Special warnings for the target species
Animals with fever and/or symptoms of an infectious disease other than trichophytosis and animals which are still under the influence of corticosteroids should not be vaccinated. Animals under 4 weeks of age should not be vaccinated. Do not vaccinate stressed animals, for example animals for which a new strawbedding has been freshly prepared.

Withdrawal periods
Edible tissue: 3 days
Milk: none

Special precautions to be taken by the person administering the product to animals
None.

Rinse with water if the vaccine is accidentally spilled onto the skin. Accidental self injection may lead to mild transient swelling at the injection site. In case of severe side effects following an accidental self injection of vaccine a medical surgeon should be consulted.

Incompatibiliti s
No incompatibility studies have been performed.

St rage
Store at between +2°C and +8°C.
Do not freeze. Protect from light.

If stored at between +2°C and +8°C and as long as the vaccine is removed from the vial correctly, the vaccine may be used for up to 14 days after the vial has been opened.

Pack sizes
50 ml, 100 ml or 250 ml glass vials.

Warnings
For animal treatment only.
Keep vaccine out of the reach of children.
Do not use vaccine after the expiry date.
Empty containers and vaccine which is no longer usable after the expiry date are to be disposed of safely according to national requirements.

Manufacturer
Serumwerke Memsen
D-27318 Hoyerhagen
Germany

Authorisation No. AR8/003/01

Boehringer Ingelheim Limited
Ellesfield Avenue
Bracknell, Berkshire
RG12 8YS

This leaflet was written in March 1998.

V 10154/IE/1

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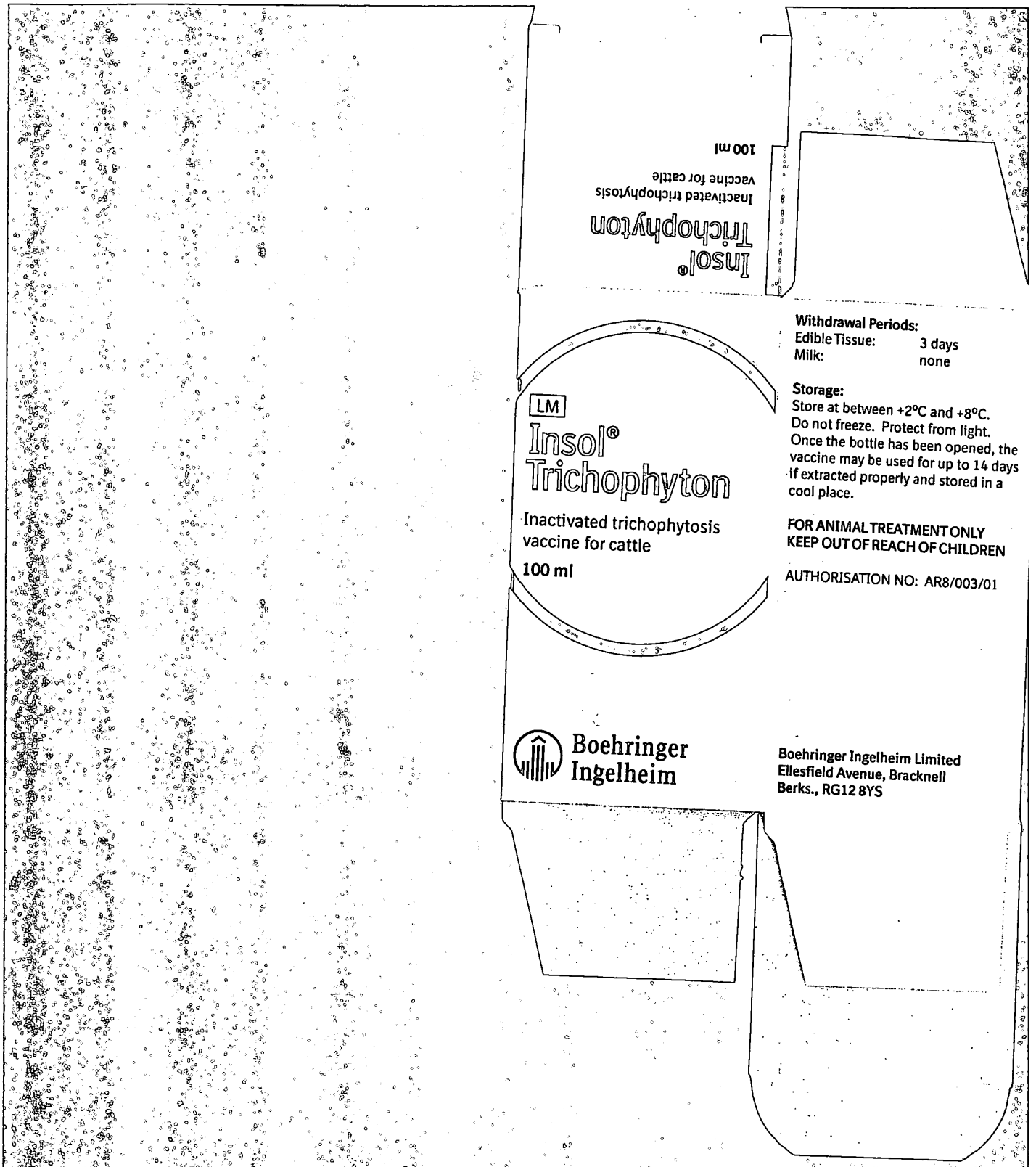
Insol®
Trichophyton
Inactivated trichophytosis
vaccine for cattle
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FOR ANIMAL TREATMENT ONLY
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AUTHORISATION NO: AR8/003/01
Boehringer Ingelheim
Boehringer Ingelheim Limited
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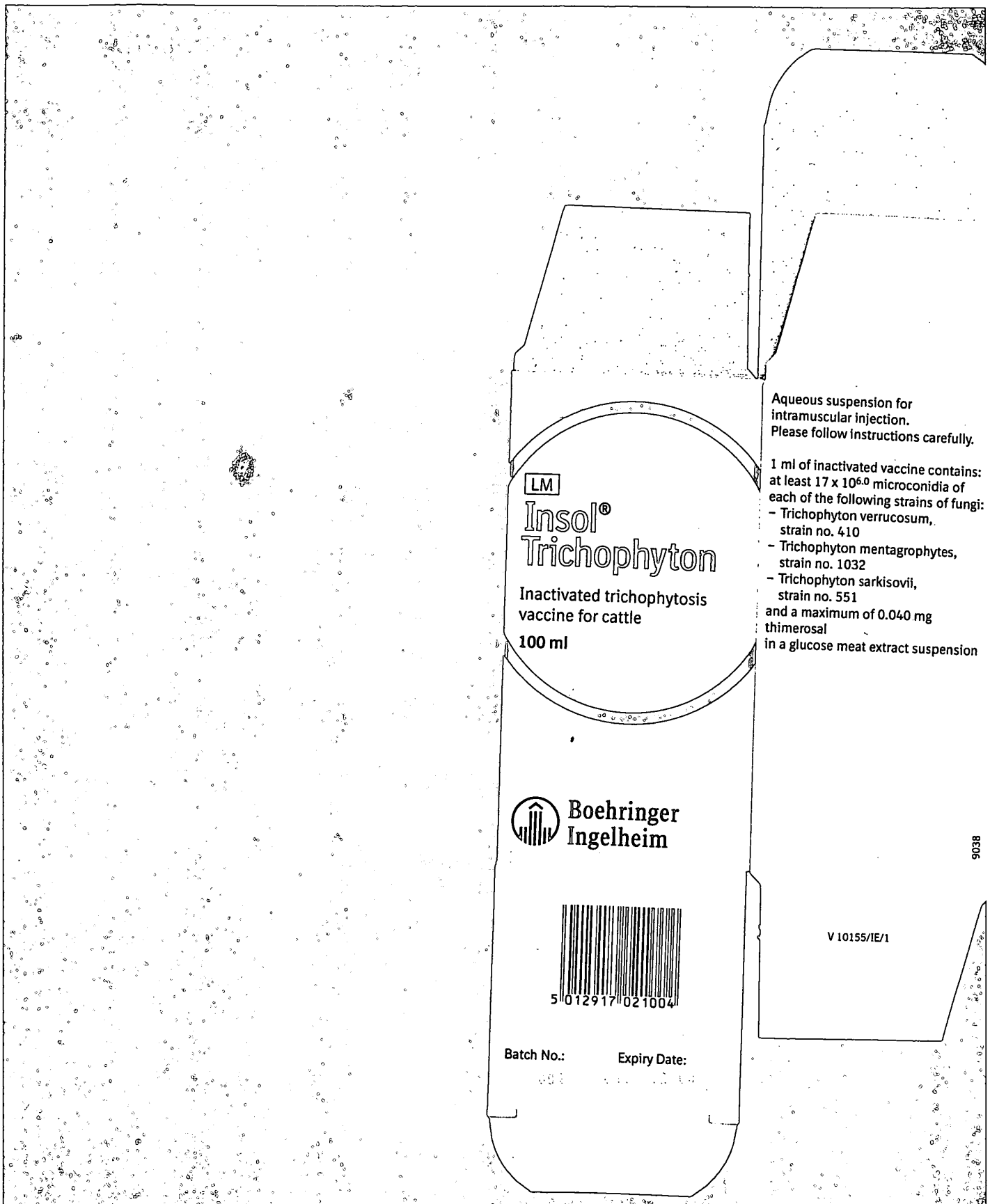
LM
Insol®
Trichophyton
Inactivated trichophytosis vaccine for cattle
100 ml
Boehringer Ingelheim
5 012917 021004
Batch No.:
Expiry Date:
Aqueous suspension for intramuscular injection.
Please follow instructions carefully.
1 ml of inactivated vaccine contains:
at least 17 x 10^6.0 microconidia of each of the following strains of fungi:
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- Trichophyton sarkisovii, strain no. 551
and a maximum of 0.040 mg thimerosal
in a glucose meat extract suspension
9038
V 10155/IE/1

APPLICANT(S):	Polyakov, I. et al
SERIAL NO.:	10/085,703
CONFIRMATION NO.:	2400
FILING DATE:	February 28, 2002
DOCKET NO.:	3/400-4-C4
TITLE:	Dermatomycosis Vaccine

IN CONNECTION WITH THE ABOVE CASE, PLEASE DATE STAMP TO ACKNOWLEDGE RECEIPT OF THE DOCUMENTS LISTED BELOW, AND RETURN TO ADDRESSEE.

1. Brief On Appeal From The Primary Examiner's Decision To The Board Of Patent Appeals And Interferences (3 Originals)
2. Exhibits A, B, C, D and E

Mailed: August 15, 2003

203

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Polyakov, I. et al
Serial No.: 10/085,703
Filed: 02/28/2002
For: Dermatomycosis Vaccine
Docket: 3/400-4-C4

Art Unit: 1645
Examiner: N. M. Minnifield

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

BRIEF ON APPEAL FROM THE PRIMARY EXAMINER'S DECISION TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Pursuant to the provisions of 35 U.S.C. § 134 and 37 C.F.R. § 1.191, applicants (hereinafter "appellants") respectfully appeal from the Primary Examiner's final rejection of all of the pending claims. A Notice of Appeal was timely filed on April 15, 2003. It is hereby requested that the time for filing this Appeal Brief be extended pursuant to 37 CFR 1.136(a) for two months, so that the extended period filing this Appeal Brief will end on August 15, 2003. Authorization is hereby given to charge the fee due under 37 C.F.R. § 1.17(c) to Deposit Account No. 02-2955, which is indicated by the enclosed Fee Transmittal Form (Form PTO/SB/17). If it is determined, however, that any additional fees under 37 C.F.R. §§ 1.16 or 1.17 are due in connection with this Appeal Brief, authorization is hereby given to charge such fees to Deposit Account No. 02-2955. This Appeal Brief is being filed in triplicate as required under 37 C.F.R. § 1.192(a).

REAL PARTY IN INTEREST

The real party in interest is Boehringer Ingelheim Vetmedica GmbH, Binger Str. 173, 55216 Ingelheim am Rhein, Germany.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any other currently pending appeal or interference that would directly affect, be affected by, or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

The instant application was filed with claims 1 and 2. Claims 1 and 2 are the subject of this appeal and set forth in the Appendix to this Appeal Brief.

STATUS OF AMENDMENTS

No amendments have been filed.

SUMMARY OF INVENTION

The instant claimed invention relates to two dermatomycosis vaccines comprising inactivated dermatophytes, wherein the inactivated dermatophytes **consist** of either eight or three specified dermatophyte strains, all of which were deposited according to the Budapest Treaty.

ISSUE PRESENTED FOR REVIEW

Whether claims 1 and 2 comply with 35 U.S.C. § 112, first paragraph.

GROUPING OF CLAIMS

Each of the two claims stand or fall independently as each claim provides different scope. Appellants therefore request that the Board independently consider the enablement of each claim in light of the arguments below.

ARGUMENT

Appellants respectfully maintain that claims 1 and 2 comply with 35 U.S.C. § 112, first paragraph, in all respects by enabling one of skill in the art to which the invention pertains to make and use the invention, as explained below. Unless indicated otherwise, all of the citations to "Office Action" below are references to the last Office Action dated February 5, 2003.

Copies of the cited Unpublished Board Opinions are enclosed for the Board's convenience. Such Unpublished Board Opinions are cited to show only the proper legal analysis and are acknowledged not to be binding precedent of the Board.

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to

enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (Office Action, page 2).

In response, appellants respectfully traverse the Examiner's rejection and maintain that the claims comply with 35 U.S.C. § 112, first paragraph, and all other statutory requirements in all respects.

In making this rejection, the Examiner has made many unsubstantiated allegations. Appellants will address each allegation made by the Examiner in order and explain why they are each either factually incorrect, legally irrelevant or improper, or both.

A. The Scope of the of Claims under Appeal

> "Where, as here, the issues presented for review concern the practical utility of the full scope of the subject matter claimed and the specification's capacity to enable one skilled in the art to make and use the full scope of the subject matter claimed, claim interpretation is a necessary prerequisite to resolution of the merits presented." (*In re Steele*, 134 U.S.P.Q. 292, 295 (CCPA 1962); *Ex parte Beck*, Appeal No. 94-3222, page 4 (UNPUBLISHED; Exhibit A); emphasis added).

Only the inventions defined by the claims need be explained in the patent application in a manner sufficient to be supported as required by 35 U.S.C. § 112, first paragraph (*Engel Industries, Inc. v. Lockformer Co.*, 20 U.S.P.Q.2d 1300, 1302 (Fed. Cir. 1991).

The claims as presented here for review each include the following clauses:

- "A dermatomycosis vaccine comprising inactivated dermatophytes": this clause indicates that the vaccine may, but does not necessarily have to comprise, in addition to the dermatophytes as specified *infra*, carriers, excipients, adjuvants etc. acceptable for and common in veterinary use as disclosed in the present specification.
- "wherein the inactivated dermatophytes **consist** of:" and listing by accession number either eight or three specified dermatophyte strains, each of which were deposited according to the Budapest Treaty. This part of the claim clearly points out that the

dermatophyte element of the vaccine as claimed is composed of only the deposited strains, see discussion *infra*.

The transitional phrase "consisting of" is close-ended and excludes any element, step, or ingredient not specified in the claim. See M.P.E.P. at § 2111.03; *In re Gray*, 11 U.S.P.Q. 255 (CCPA 1931); *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (Bd. App. 1948). When the phrase "consists of" appears in a clause of the body of a claim, rather than immediately following the preamble, it limits only the element set forth in that clause, other elements are not excluded from the claim as a whole. See M.P.E.P. § 2111.03; *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 230 U.S.P.Q. 45 (Fed. Cir. 1986).

Thus, claim 1 must be interpreted to include no less and no more than the following dermatophytes:

- *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277)
- *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279)
- *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278)
- *Trichophyton equinum* Strain No. VKPGF-929/381 (accession No. DSM 7276)
- *Microsporum canis* Strain No. VKPGF-928/1393 (accession No. DSM 7281)
- *Microsporum canis var. obesum* Strain No. VKPGF-727/1311 (accession No. DSM 7280)
- *Microsporum canis var. distortum* Strain No. VKPGF-728/120 (accession No. DSM 7275)
- *Microsporum gypseum* Strain No. VKPGF-729/59 (accession No. DSM 7274).

Similarly, claim 2 must be interpreted to include no less and no more than the following dermatophytes:

- *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277)
- *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279)
- *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278).

B. Appellants Have Taught How to Make the Vaccines within the Scope of the Claims

This fact is undisputed by the Examiner:

> "The Examiner agrees that the specification teaches how to make the claimed vaccine" (Office Action at page 3, last paragraph).

C. Appellants have Taught how to Use the Vaccines within the Scope of the Claims

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement". *In re Wright*, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993)(emphasis added). See also *In re Morehouse*, U.S.P.Q. 29, 32 (CCPA 1976); *Ex parte Charoenvit*, Appeal No. 1999-1413 (UNPUBLISHED; Exhibit B). The Examiner's conclusory statement "The rejection is maintained for the reasons of record" only accompanied by unsupported allegations not relating to the present claims does not satisfy this burden.

Upon careful review of the previous Office Action dated May 30, 2002, no proper explanation or sufficient reasons were given by the Examiner as to why the scope of protection provided by the claim is allegedly not enabled by the specification.

As no sufficient reasons can be found in either one of the Office Actions, the Office Actions regarding the parent application 09/256,915, to which benefit is claimed in the subject application, were reviewed. Quite surprisingly, the same examiner acknowledged the enablement for the use of the inactivated strain in a vaccine composition:

> "Claim 18, 21-23, 34 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for use of the inactivated strain**, does not reasonably provide enablement for one antigen from the dermatophytes, T. verrucosum, to be used in the vaccine composition." (Final Office Action dated August 29, 2003, page 3 at 6.; emphasis added)

Appellants fully agree with Examiner's conclusion that the specification is fully enabling for the use of any of the inactivated strains. Accordingly, if the use of a vaccine containing only one inactivated strain is considered to be disclosed in an enabling manner, how can the use of a vaccine containing eight or three of such strains not be considered to be disclosed in an enabling manner?

In short, if a vaccine comprising one strain is shown to provide immunity and to comply with the requirements of 35 U.S.C. 112, first paragraph, why should a vaccine comprising several of said strains not provide immunity?

The Examiner put forward several, unsupported allegations as discussed below:

(a) "It is not clear what Applicants used in the vaccine composition. Example 1, page 18 indicates that "[A]fter 2 days, 125 ml of each culture in suspension is taken and mixed in a single container. The vaccine may be prepared by mixing together various combinations of the given strains." Exactly what was the composition of the vaccine administered that gave the results found in Tables 9 and 10? It is not clear if all 8 dermatophytes were used or some combinations of 3, 4, 6 or 7 dermatophytes. It is not clear that the specific combination of 3 dermatophytes as set forth in claim 2 were used." (Office Action at page 2, 4. to page 3, first paragraph).

(b) "Specifically, the specification has not taught how to use the claimed vaccine. Mixing each culture in a single container or mixing together various combinations of the given cultures is set forth. However, it is not clear which composition (all 8 cultures in one container or various combinations of less than 8 cultures and if less than 8 cultures specifically which ones) was used to generate the data found on tables 9 and 10 of the specification." (Office Action at page 3, last paragraph to page 4, first paragraph).

(c) "Does Applicant intend for "immunogenic response" to mean that vaccine protection has been established, see page 11?" (Office Action at page 3, first paragraph). "Does the vaccine comprising a combination of cultures protect in the same manner as the individual cultures; is there a synergistic affect with regard to protection against ringworm infection?" The Examiner further cites Gudding et al (Can. Vet. J. 1995) and continues "Further, the inactivated vaccine against ringworm must be capable of eliciting both humoral and cellular immune responses, of which the cellular immune response is crucial for protection and adjuvants are important in stimulating the cellular branch of the immune system (pp. 303-304). In view of the state of the art it is not clear if protection has been established against ringworm infection when Applicants state (see tables 1-7) "establishes immunity". It is not clear what type of immunity is established. Applicant's vaccine composition does not recite a carrier or adjuvant, however Gudding indicates that the adjuvants are important in stimulating the cellular branch of the immune system and the cellular branch is crucial for protection.

Allegation (a)

With regard to allegation (a), the Examiner has cited only part of Example 1. Omitted is the preceding paragraph:

> "To produce 1 liter of vaccine, cultures are taken of the strains VKPGF-931/410, 930/1032, 929/381, 551/68, 928/1393, 727/1311, 728/120, and 729/59 and grown in agar/wort at 26°C for 15 days. Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer. The solution used is an aqueous solution containing 1% fermented hydrolyzed muscle protein, 10% glucose and 1% yeast extract. The concentration of microconidia is brought to 90 million per ml of homogenate. After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container." (emphasis added).

Therefore, from the quoted wording, it is clear to the skilled person that in cited Example 1 the 8-fold vaccine, exactly as claimed in claim 1, was prepared and used in prophylaxis and therapy.

The sentence "The vaccine may be prepared by mixing together various combinations of the given strains" (emphasis added), uses the term "may" which clearly indicates to the skilled person what optionally may be done, e.g. instead of eight claims, the combination of three strains as recited in claim 2 may be used in a vaccine according to the invention.

Allegation (b)

Regarding allegation (b), the wording of example 1 clearly states that each of the eight cultures is first cultured separately and homogenized:

> "Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer."

and then combined into one container:

> "After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container."

Further, the specification extensively describes immunizing the animals using the vaccine prepared in Example 1 to determine dosage to be given and the method of administration for prevention and treatment in ten different animal families (page 18, line 33 and Table 8). The effectiveness of the vaccine in preventing disease in 24 animal species is given (Example 2, page 21, and Table 9); and the effectiveness of the vaccine in treating infected animals in 18 different animal species is provided (Example 3, page 21 and Table 10).

Furthermore, clarification can also be drawn from page 3, lines 5-12 and 20-22 disclosing preferred vaccine combinations in the context of page 4, lines 8-18:

Page 3, lines 5-12:

> This aim has been achieved by using the following fungal strains as vaccinal strains: *Trichophyton verrucosum* (especially No. VKPGF-931/410), *Trichophyton mentagrophytes* (especially No. VKPGF-930/1032), *Trichophyton equinum* (especially No. VKPGF-929/381), *Trichophyton sarkisovii* (especially No. VKPGF-551/68), *Microsporum canis* (especially No. VKPGF-928/1393), *Microsporum canis var. obesum* (especially No. VKPGF-727/1311),

Microsporum canis var. distortum (especially No. VKPGF-728/120), *Microsporum gypseum* (especially No. VKPGF-729/59). Vaccines can be produced by using various combinations of antigenic material from the above strains together with a suitable carrier.

Page 3, lines 20-22:

"Another preferred combination of vaccine strains consists of *Trichophyton verrucosum* No. VKPGF-931/410, *Trichophyton mentagrophytes* No. VKPGF-930/1032, *Trichophyton sarkisovii* No. VKPGF-551/68, particularly for use in cattle."

Page 4, lines 8-18:

In order to prepare a vaccine the following procedure may be used, for example:

Cultures of the strains are homogenized in an aqueous solution containing 0.2 ti 2.0% fermented, hydrolyzed muscle protein (FGM-s), 5 to 12% glucose and 0.1 to 1.2% yeast extract. The concentration of the microconidia is adjusted to 40 to 120 million per milliliter and after 1 to 2 days the mixture is inactivated, *e.g.*, with thiomersal ($C_9H_9O_2SNaHg$) in the ration 1:10,000 to 1:25,000, or with another substance known from the prior art. The resulting suspension is packaged and is ready for use in animals.

The preparation of the vaccines, the dosage to be given and the method of administration for prevention and therapeutic treatment are explained in Examples 1 to 3.

With the before-mentioned extensive guidance provided to the skilled person, appellants have shown how to make and use both vaccines within the scope of the claims, including claim 2.

Furthermore, the Examiner did not consider and apply the factors and analysis of *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) and *Ex parte Forman*, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). In properly considering and applying the factors concerning enablement, the following factors should be considered: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

With regard to factors (1) and (2), to practice the invention, either 8 or 3 dermatophytes must be grown, mixed together in a single container, the mixture is inactivated, and the resulting vaccine is bottled (described in the specification on pages 4, lines 10-18, page 18, lines 15-31), and applied to animals at a dosage and with a route of administration as disclosed in Example 2, page 21, and Table 9 (prevention) as well as Example 3, page 21 and Table 10 (therapy). As set out *supra*, the dosage and route of administration is given for 10 different animal families, and guidance regarding efficacy of the 8-fold vaccine is given for 24 animal species (prevention) and 18 animal species (therapy) all of which represents a very limited amount of routine experimentation under a significant amount of guidance presented in the specification. If at all, there is minimal routine experimentation necessary to test the 3-fold vaccine in a similar manner as the 8-fold vaccine. With regard to factor (3), there are several in-depth working examples disclosing the preparation of vaccines according to the invention, the dosage, the route of preventive or therapeutic administration for numerous animal species. With regard to factors (4), (5), (6), and (7), as the nature of the invention is in the immunology, animal health and vaccine art, which is very highly developed, the state of the prior art is high, and the relative skill of those in the art is at a very high level, one would expect one of skill in the art would easily be able to use the directions in the specification to make and use the vaccines according to the invention. Regarding factor (8), it should be pointed out again that the claims presented for review are not generic claims, but are directed to two specific vaccines consisting of eight or three specified dermatophytes.

This situation is in contrast to that of *Ex parte Forman*, where the art was "undeveloped", that at the time (early 1980s) "experiments in genetic engineering produce, at best, unpredictable results", there were no apparent reproducible working examples presented outside the scope of the deposited microorganism strains, nor did there "appear to be ... a single detailed example that could be followed by another worker in another lab to obtain a single specific microorganism (vaccine) within appellants' claims, without recourse to the deposited strains recited in the allowed claims." *Ex parte Forman*, at 548. The instant situation is more like *In re Wands*, where enablement was shown, as appellants' disclosure, like Wands' disclosure, "provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *In re Wands* at 1406.

35 U.S.C. § 112, first paragraph, certainly does not require each and every embodiment of the invention to be exemplified. Even the lack of a working example (quite contrary to the situation here with several working examples), if all the other factors point to enablement, is not considered to render the invention non-enabled, if one skilled in the art will be able to practice it without an undue amount of experimentation (M.P.E.P. 2164.02; *In re Borkowski*, 164 U.S.P.Q. 642, 645 (CCPA 1970).

Further, the test is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue (M.P.E.P. § 2164.01; *In re Angstadt*, 190 U.S.P.Q. 214, 219 (CCPA 1976); *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, U.S.P.Q. 409, 413 (Fed. Cir. 1984).

The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *The Johns Hopkins University v. Cellpro Inc.* 47 U.S.P.Q.2d 1705, 1719; *PPG Indus., Inc. v. Guardian Indus. Corp.* 37 U.S.P.Q.2d 1618, 1623 (emphasis added).

With the significant amount of guidance presented in the specification, the minimal routine experimentation necessary to test the 3-fold vaccine in a similar manner as the 8-fold vaccine can certainly not be considered undue.

Allegation (c)

With regard to allegation (c), appellants cite Taber's cyclopedic medical dictionary, in existence since 1940 and clearly the standard to the skilled person (Exhibit C). It is appropriate to compare the meaning of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. *In re Barr*, 170 U.S.P.Q. 330 (CCPA 1971).

"Vaccine" is defined to be used as follows:

> "FUNCTION: Vaccines are used to stimulate **an immune response** in the body by creating antibodies **or** activated T lymphocytes capable of controlling the organism. **The result is protection against disease**; the duration depends on the particular vaccine. (emphasis added)"

Therefore, for the use of a vaccine to be enabled, it is fully sufficient to stimulate an immune response which can either be the generation of antibodies or activated T lymphocytes, both requirements do not need to be satisfied. The Examiner's arbitrary requirement of requiring both humoral (antibody-mediated) and cellular (T lymphocyte) responses is neither scientifically justified nor founded in the law. To fulfil the requirements of 35 U.S.C. § 112, first paragraph, it is fully sufficent that the vaccines according to the invention provide an immune response. This is extensively exemplified in Examples 2 and 3, page 21, and Tables 9 and 10 of the specification.

Likewise, the Examiner's arbitrary requirement for an adjuvant to be present in the vaccine is neither scientifically justified nor founded in the law as discussed *infra*. Appellants successfully sell Insol® Dermatophyton and Insol® Trichophyton, wherein the dermatophytes consist of the strains as claimed in claim 1 and 2 presented for review (package inserts presented in Exhibits D and E, respectively). Both vaccines do not require adjuvants due to the superior properties of the vaccine strains contained therein. Thus, it is again respectfully submitted that the subject matter claimed fully complies with the requirements set forth in 35 U.S.C. § 112, first paragraph.

In many of these allegations, the Examiner seems to be attempting to shift the burden to the appellants to affirmatively prove that appellants are entitled to a patent, when it is the Examiner's burden to prove that appellants are not entitled to a patent with rejections that are supported by evidence and a rational basis. This the Examiner has not done.

Appellants contend that the legal standard is whether a claim is understandable to one of ordinary skill in the art and that it defines subject matter that appellants regard as the invention. Federal Circuit cases have made clear that claim language must not be analyzed in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings in the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *In re Marosi*, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 221 U.S.P.Q. 1 (Fed.Cir.1983); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed.Cir.1983).

In conclusion, appellants have shown by description and examples how to produce the vaccines according to the invention, and also how to use the vaccines for prophylaxis and therapy in numerous animal species. Accordingly, appellants have shown how to make and use both vaccines within the scope of the claims.

Accordingly, appellants submit that, based on the arguments above, claims 1 and 2, comply with 35 U.S.C. § 112, first paragraph, as well as with all other statutory requirements of the U.S. Patent Law. An applicant who complies with the statutory requirements is entitled to a patent. *In re Rouffet*, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998); *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992); *In re Grabiak*, 226 U.S.P.Q. 870, 873 (Fed. Cir. 1985); *In re Rinehart*, 189 U.S.P.Q. 143, 147 (C.C.P.A. 1976).

Consequently, appellants respectfully maintain that the Examiner's rejections of pending claims 1 and 2 were improper, and request that the Board reverse all of the appealed rejections and direct the Examiner to issue a Notice of Allowance for all of the pending claims.

APPENDIX

The following claims 1 and 2 are on appeal.

1. A dermatomycosis vaccine comprising inactivated dermatophytes, wherein the inactivated dermatophytes consist of: *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277), *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279), *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278), *Trichophyton equinum* Strain No. VKPGF-929/381 (accession No. DSM 7276), *Microsporum canis* Strain No. VKPGF-928/1393 (accession No. DSM 7281), *Microsporum canis var. obesum* Strain No. VKPGF-727/1311 (accession No. DSM 7280), *Microsporum canis var. distortum* Strain No. VKPGF-728/120 (accession No. DSM 7275), and *Microsporum gypseum* Strain No. VKPGF-729/59 (accession No. DSM 7274).

2. A dermatomycosis vaccine comprising inactivated dermatophytes, wherein the inactivated dermatophytes consist of: *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277), *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279), and *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278).

Certificate of Mailing Under 37 C.F.R. § 1.8(a)
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on August 15, 2003.

Susan K. Pocchiari

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August 15, 2003

Dated

Respectfully submitted,

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THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today
(1) was not written for publication in a law journal and
(2) is not binding precedent of the Board.

Paper No. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LEE R. BECK and RALPH J. STOLLE

Appeal No. 94-3222
Application 07/815,630[1]

HEARING: July 16, 1998

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[1] Application for patent filed December 30, 1991. According to applicants, this application is a continuation of Application 07/548,419, filed July 5, 1990, now abandoned; which is (1) a continuation-in-part of Application 07/431,639, filed November 6, 1989, now U.S. 5,130,128, issued July 14, 1992; and (2) a continuation-in-part of Application 07/177,223, filed April 4, 1988, now U.S. 4,956,349, issued September 11, 1990. Application 07/431,639 is a continuation-in-part of Application 07/161,039, filed February 26, 1988, now U.S. 4,879,110, issued November 7, 1989. Both Applications 07/161,039 and 07/177,223 are continuations-in-part of Application 07/001,848, filed January 9, 1987, now U.S. 4,897,265, issued January 30, 1990; which is a divisional of Application 06/546,162, filed October 27, 1983, now U.S. 4,636,384, issued October 23, 1990; which is a continuation-in-part of Application 06/384,625, filed June 3, 1982, now abandoned. U.S. 4,636,384 was reissued as U.S. Re. 33,403 on October 23, 1990.

Before WINTERS, WILLIAM F. SMITH, and GRON, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

This is an appeal under 35 U.S.C. § 134 from an examiner's final rejection of Claims 2 and 6-9.

On consideration of the record of this case in its entirety, it is hereby ORDERED that

the examiner's final rejections in this case are VACATED, and that

this application is REMANDED to the examiner for further action consistent with the following opinion.

1. Introduction

Claims 1-9 are pending in this application. In accordance with 37 CFR § 1.142(b), Claims 1 and 3-5 have been withdrawn from further consideration by the examiner as directed to non-elected subject matter under a restriction requirement. Claims 2 and 6-9 stand rejected as unpatentable under 35 U.S.C. § 101 purportedly as drawn to subject matter without practical utility and under

35 U.S.C. § 112, first paragraph, as supported by a specification which purportedly would not have enabled persons skilled in the art to use the full scope of products and methods claimed for the utility indicated.

According to appellants, Claims 2 and 6-9 stand or fall together (Brief on Appeal, p. 4). Claims 2 and 6 represent the subject matter claimed and read:

> 2. A food product comprising a composition wherein said composition comprises a non-antibody fraction of milk and wherein said non-antibody fraction of milk ameliorates, in a subject with an allergy to an allergen, the symptoms of said allergy of said subject to said allergen when said fraction is ingested by said subject and wherein said fraction is produced by the process comprising:
>
> (a) administering said allergy to a milk-producing animal;
>
> (b) collecting the milk from said animal of part (a);
>
> (c) filtering the milk of part (b) through a filter which excludes molecules of greater than 100,000 daltons; and
>
> (d) collecting the effluent from the filtration of part (c) wherein said effluent contains said fraction.
>
> 6. A method for desensitizing a subject to an allergen wherein said method comprises orally administering to said subject a food product, in an amount and for a time sufficient to produce an amelioration in said subject of

symptoms of allergy to said allergen, wherein said food product comprises a non-antibody fraction of milk from a milk-producing animal that has been immunized with said allergen.

2. Discussion

It should have been apparent from the questions this panel of the Board asked counsel at Oral Hearing on July 16, 1998, that we should not rule on the merits of this appeal because, as a matter of law, it would be incorrect to do so. Accordingly, we vacate the examiner's decision finally rejecting the subject matter on appeal under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, for reasons which follow.

We have searched the record of this case and do not find any indication that the metes and bounds of the subject matter claimed have been established. Where, as here, the issues presented for our review concern the practical utility of the full scope of the subject matter claimed and the specification's capacity to enable one skilled in the art to make and use the full scope of the subject matter claimed, claim interpretation is a necessary prerequisite to resolution of the merits of the issues presented. See In re Steele, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962)(When an analysis

of the claims leaves the reviewing body in a quandary as to what they cover, the examiner and the Board may not rely on speculation as to the meaning of the claims in support of a rejection.) In re Moore, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971) instructs at 1235, 169 USPQ at 238 [footnotes omitted]:

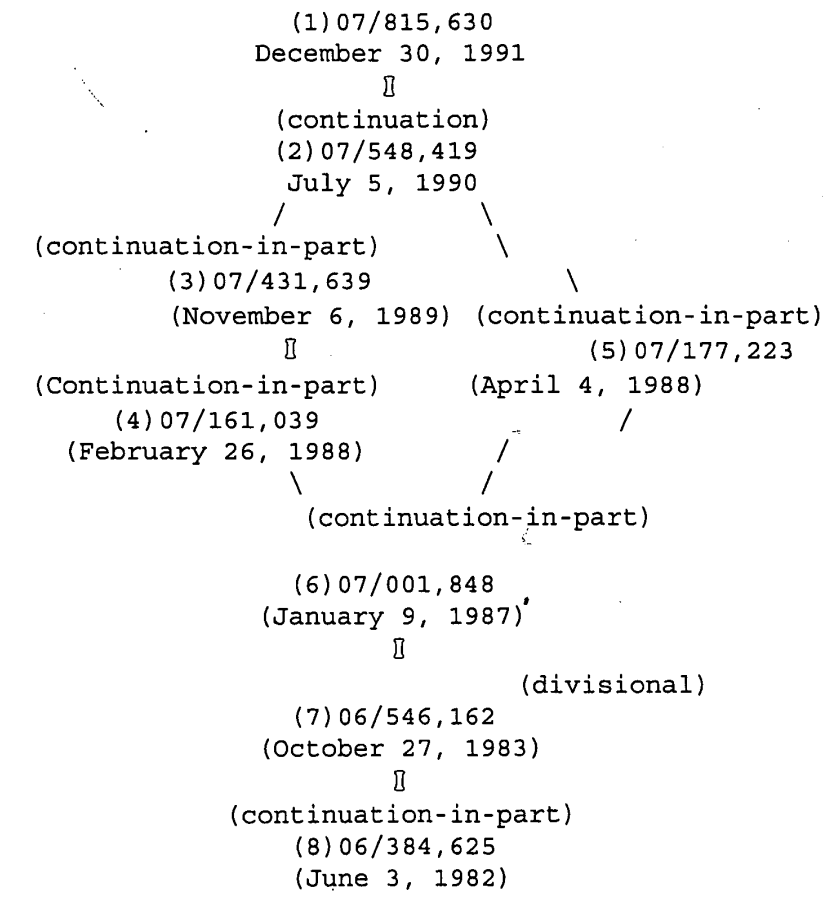
> [The] . . . first inquiry therefore is merely to determine whether the claims do . . . set out and circumscribe a particular area with a reasonable degree of precision and particularity. It is here where the definiteness of the language employed must be analyzed--not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.
>
> Once having determined that the subject matter defined by the claims is particular and definite, the analysis then turns to the first paragraph of section 112 to determine whether the scope of protection sought is supported and justified by the specification disclosure.

For example, the examiner appears not to have interpreted the term "allergen" in Claims 2 and 6, the phrases "allergy to an allergen" in Claim 2 and "allergy to said allergen" in Claim 6, the phrases "ameliorates . . . the symptoms of said allergy" in Claim 2 and "an amelioration . . . of symptoms of allergy" in Claim 6, the term "non-antibody fraction" in Claims 2 and 6, the phrase "a non-antibody fraction of milk from a milk-producing animal that has been immunized with said

allergen" in Claim 6 (emphasis added), and the phrase "excludes molecules of greater than 100,000 daltons" in Claim 2. We will refrain from considering the patentability of the claimed subject matter under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, until the examiner has first interpreted the meaning and breadth of the aforementioned terms and phrases in light of the description of the claimed subject matter in the specification and the teachings of the prior art. Id. at 1235, 169 USPQ at 238.

Moreover, we do not understand how it is possible for the examiner of this application to consider the meaning and breadth of the terms and phrases in appellants' claims in light of the prior art or to determine whether this specification would have enabled persons skilled in the art at the pertinent time to make and use the full scope of invention claimed without having first determined the effective filing date of the subject matter claimed. Unless and until the effective filing date of the subject matter presently claimed is established, what is and what is not prior art as to the subject matter presently claimed can be no more than speculative.

For example, applicants claim the benefit of priority under 35 U.S.C. § 120 through two lineages (Spec., p. 1, first para.):



With those two lines in mind, we list the following information:

(1) Application 07/815,630 for "IMMUNE SUPPRESSIVE PRODUCT," was filed December 30, 1991, in the names of Beck and Stolle.

(2) Application 07/548,419 was filed July 5, 1990, also in the names of Beck and Stolle and is said to be the parent of continuation Application 07/815,630 (this application);

(3) Application 07/431,639 for "USE OF HONEY AS VACCINE" was filed November 6, 1989, in the sole name of Stolle and issued July 14, 1992, as U.S. 5,130,128;

(4) Application 07/161,039 for "ANTIHYPERTENSIVE HYPERIMMUNE MILK, PRODUCTION, COMPOSITION, AND USE" was filed February 26, 1988, in the names of Beck and Stolle and issued November 7, 1989, as U.S. 4,879,110;

(5) Application 07/177,223 for "ANTI-INFLAMMATORY FACTOR, METHOD OF ISOLATION, AND USE" was filed April 4, 1988, in the sole name of Beck and issued September 11, 1990, as U.S. 4,956,349;

(6) Application 07/001,848 for "METHOD FOR TREATING DISORDERS OF THE VASCULAR AND PULMONARY SYSTEMS" was filed January 9, 1987, in the names of Stolle and Beck and issued January 30, 1990, as U.S. 4,897,265;

(7) Application 07/546,162 for "METHOD FOR TREATING DISORDERS OF THE VASCULAR AND PULMONARY SYSTEMS" was filed October 27, 1983, in the names of Stolle and Beck and issued January 13, 1987, as U.S. 4,636,384; and

(8) Application 07/384,625, now abandoned, was filed June 3, 1982, in the names of Stolle and Beck.

We note from the above listing that while the subject matter appellants claim appears to be entitled to the July 5, 1990, filing date of (2) Application 07/548,419 filed in the names of Beck and Stolle as a file-wrapper continuation of this application, it is not at all apparent that the full scope of the subject matter presently claimed is entitled either to the November 6, 1989, filing date of (3) Application 07/431,639 for "USE OF HONEY AS VACCINE" filed in the sole name of Stolle or the April 4, 1988, filing date or (5) Application 07/177,223 for "ANTI-INFLAMMATORY FACTOR, METHOD OF ISOLATION, AND USE" filed in the sole name of Beck. In fact, this record is noticeably devoid of any indication that the effective filing date of the subject matter claimed has been determined. Accordingly, it is our view that claim interpretation in light of the prior art cannot have been adequately done without first determining the merits of

applicants' claims under 35 U.S.C. § 120 so as to enable one to establish what constitutes the prior art under 35 U.S.C. § 102.

Moreover, while compliance with the requirements of 35 U.S.C. § 112, first paragraph, is normally determined as of the filing date of the pending application, the examiner, when faced with an intervening reference, may be required to focus on the filing date of a prior application as the result of the applicants' claims for priority under 35 U.S.C. § 120. United States Steel Corp. v. Phillips Petroleum Co., 865 F.2d 1247, 1251, 9 USPQ2d 1461, 1464 (Fed. Cir. 1989). We appear to have just such a case before us.

On their face, Stolle, U.S. 5,130,128, filed November 6, 1989, and Beck, U.S. 4,956,349, filed April 4, 1988, appear to be prior art under 35 U.S.C. § 102(e) whether or not they are commonly assigned with this application filed in the names of Beck and Stolle. See In re Bartfeld, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991). Moreover, Stolle and Beck, U.S. 4,636,384 and U.S. 4,732,757 may be prior art under 35 U.S.C. § 102(b). Accordingly, faced with what prima facie appears at least in part to be prior art of record and applicants' claims for priority under 35 U.S.C. § 120 in this case, the examiner

should determine the effective filing date of the subject matter here claimed before ruling on patentability under either 35 U.S.C. § 112, first paragraph, § 101, § 102, or § 103. It is as of the effective filing date that compliance with 35 U.S.C. §§ 112, first paragraph, and 101 and prior art availability must be determined.

Only after determining the effective filing date of the subject matter claimed may the examiner (1) determine whether appellants' claims satisfy 35 U.S.C. § 112, second paragraph, in light of applicants' disclosure and the prior art, (2) consider whether the subject matter claimed is patentable under 35 U.S.C. § 101 or whether applicants' disclosure would have enabled one skilled in the art to make and use the full scope of the claimed subject matter as required by 35 U.S.C. § 112, first paragraph, (3) determine patentability under 35 U.S.C. §§ 102 and 103 in view of the prior art (compare Chester v. Miller, 906 F.2d 1574, 1576, 15 USPQ2d 1333, 1336 (Fed. Cir. 1990), citing In re Gosteli, 872 F.2d 1008, 1010-1011, 10 USPQ2d 1614, 1616 (Fed. Cir. 1989)), and (4) determine whether the subject matter claimed in this case is unpatentable for obviousness-type

double-patenting of subject matter claimed in any one or more of the U.S. patents which have issued from applications for which

priority under 35 U.S.C. § 120 here is claimed.[2]

We will allow the examiner of this case to determine in the first instance the effective filing date of the subject matter claimed, the scope and content of the pertinent prior art, compliance with the requirements of the second paragraph of Section 112, compliance with Section 101 and the first paragraph of Section 112, and patentability of the claimed subject matter under 35 U.S.C. § 102, under 35 U.S.C. § 103, and over subject matter claimed in commonly assigned patents absent the filing of effective terminal disclaimers. For this panel to review the merits of the examiner's decision rejecting the claims on appeal under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, at this time without those preliminary determinations having been made by an examiner is

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[2] The examiner may wish to consider obviousness-type double-patenting issues. However, take note that if questions of obviousness-type double patenting of subject matter claimed in issued patents come to light, the examiner may want to consider whether adhering to unpatentability determinations under 35 U.S.C. § 101 or 112, first paragraph, for lack of utility is consistent with the presumption of validity of the patented subject matter.

inconsistent with our review function. See 35 U.S.C. § 7 ("The Board . . . shall . . . review adverse decisions of examiners . . . .") Accordingly, we vacate the examiner's final rejections and remand the case to the examining corps for action consistent with this opinion.

This application, by virtue of its "special" status, requires an immediate action, M.P.E.P. § 708.01(d). It is important that the Board be informed promptly of any action affecting the appeal in this case.

VACATED and REMANDED

SHERMAN D. WINTERS Administrative Patent Judge	)
WILLIAM F. SMITH Administrative Patent Judge	) BOARD OF PATENT APPEALS AND INTERFERENCES
TEDDY S. GRON	)

Administrative Patent Judge)

Appeal No. 94-3222
Application 07/815,630

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Washington, DC 20005-3934

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte YUPIN CHAROENVIT, STEPHEN L. HOFFMAN,
RICHARD L. BEAUDOIN, DECEASED, BY BARBARA A. BEAUDOIN

Appeal No. 1999-1413
Application No. 08/176,024

ON BRIEF

Before SCHEINER, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

[redacted]

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 7, 11, and 12, which are all of the claims pending in the application.

Claims 1, 4, and 11 are representative and read as follows:

1. A formulation protective against Plasmodium vivax for a time commensurate with the time monoclonal antibody Navy Vivax Sporozoite 3 (HB10615) remains at pharmacologically active levels in a subject's blood stream, comprising a pharmaceutical amount sufficient to provide passive immunization of Navy Vivax Sporozoite 3 (HB10615) in a pharmaceutically suitable injectable solution.

4. A method of providing protection from Plasmodium vivax induced malaria for subjects experiencing exposure to infected mosquitoes, for a time commensurate with the time monoclonal antibody Navy Vivax Sporozoite 3 (HB 10615) remains at pharmacologically active levels in a subject's blood stream, that comprises introducing and circulating the antibody Navy Vivax Sporozoite 3 (HB 10615) in the subject's blood stream.

11. A humanized antibody capable of providing passive protection against Plasmodium vivax wherein said antibody has a variable region comprising the hyper variable regions of the heavy and light chains of monoclonal antibody Navy Sporozoite 3 (HB10615) and human antibody framework regions.

The examiner relies on the following references:

McCutchan et al (McCutchan 1) 4,694,944 Sept. 15, 1987

McCutchan, T.F. et al (McCutchan 2). "Sequence of the Immunodominant Epitope for the Surface Protein Sporozoites of Plasmodium vivax," Science, Vol. 23, pp. 1381-1383 (1985)

Harlow et al. (Harlow), Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory pp. 287 (1988)

Charoenvit, Y. et al. (Charoenvit), "Inability of Malaria Vaccine to Induce Antibodies to a Protective Epitope Within its Sequence," Science, Vol. 251, pp. 668-671 (1991)

[redacted]

Harris et al. (Harris), "Therapeutic Antibodies - The Coming of Age," Tibtech, Vol. 11, pp. 42-44 (1993)

Mitchell, G. H., (Mitchell), "An Update on Candidate Malaria Vaccines," Parasitology, Vol. 98, New York, pp. S29-S46 (1989)

Grounds of Rejection

1. Claims 1-3 stand rejected under 35 U.S.C. §103. As evidence of obviousness, the examiner cites McCutchan (1 and 2) and Harlow.

2. Claims 1-7, 11 and 12 stand rejected under 35 U.S.C. §112, first paragraph. As evidence of nonenablement, the examiner cites Charoenvit, Harris, and Mitchell.

We reverse both rejections.

DISCUSSION

Procedural Matters

In this case, an Appeal Brief with four attached 1.132 declarations was filed concurrent with a proposed amendment, on March 1, 1996. After several interviews and written communications, amended claims were entered by the Examiner, the effect of amendment entry on the rejections of record was communicated to the appellant on August 21, 1996, and a Substitute Brief was filed September 20, 1996, containing arguments directed to the amended claims. The Substitute Brief also refers to the

declarations by Drs. Steven L. Hoffman (1st and 2nd declarations), Yupin Charoenvit, and Thomas F. McCutchan, which were attached to the original Brief.

In the Examiner's Answer, four rejections under 35 U.S.C. § 103 were withdrawn. No new grounds of rejection were made, and no Reply Brief was filed.

Background

Plasmodium vivax is one of the four species of parasite causing malaria in humans (specification, page 1). Despite major efforts over at least 20 years, a commercially viable malaria vaccine has not been achieved (page 2 of the December 28, 1993 amendment to the specification). The present invention involves a monoclonal antibody, here designated NVS3. The monoclonal antibody has been described in the prior art (specification, page 2). This antibody binds to an epitope within a repeated nine amino acid sequence of the circumsporozoite protein of P. vivax (specification, page 8). Prior to the invention, recombinant proteins comprising the P. vivax repeated amino acid sequence failed to induce a significant protective effect in Saimiri monkeys in active immunization experiments (specification, pages 3-4). An object of this invention is to provide passive protection against P. vivax by administering the antibody to a subject, where the antibodies

bind to P. vivax sporozoites in the circulation of the host and render the sporozoites noninfectious thereby preventing malarial disease (specification, pages 4 and 7-8).

Enablement

Claims 1-7, 11 and 12 stand rejected under 35 U.S.C. §112, first paragraph. As evidence of nonenablement, the examiner cites Charoenvit, Harris, and Mitchell.

Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." In re Wands, 858 F.2d 73, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie

case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F2d 162, 165, 192 USPQ 29, 32 (CCPA 1976). The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement.

Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In the present case, the examiner cites the state of the art and the lack of working examples involving humans as the factors leading to a conclusion of non-enablement. Specifically, the examiner argues (Answer, page 6):

> The state of the art to which the invention pertains is such that as of this date passive immunization has not been used to prevent malaria in humans and that there are no vaccines for active or passive immunization that are accepted as being effective for prevention of P. vivax malaria. Charoenvit et al. (Science 251) states that it has never been definitively established in humans that circulating antibodies to the sporozoite of Plasmodium can prevent infection. Furthermore, Harris et al. establishes the use of monoclonal antibodies for in vivo human therapy is art-recognized to be highly experimental and unpredictable to those of skill in the art. The record contains no working examples relating to the use of the NVS3 antibody for treatment of P. vivax malaria in humans....
>
> The invention has been exemplified using the monkey model. However, the evidence obtained using the monkey model is not sufficient to allow one of ordinary skill in the art to predict the ability to practice the claimed invention for treatment of humans given that the monkey model used to exemplify the claimed invention is not an art-accepted model which is recognized as having a clear correlation with human efficacy for the evaluation of agents for passive immunotherapy of malaria.

On the other hand, the appellants argue that proof of efficacy in humans is not required, and that the monkey animal model tests disclosed in the specification are accepted by experts in the field. Substitute Brief, pages 13-15.

The specification provides a working example demonstrating efficacy of the claimed formulation in a nonhuman primate, the Saimiri monkey. Example 3, pages 13-15. In addition, the Hoffman Declaration of record provides an expert opinion that "most experts in the field consider this monkey model to be the most reliable system for predicting what will occur in humans." Hoffman Declaration, page 6. The Hoffman Declaration also cites long-held knowledge in the art of passive immunotherapy for acute malaria in human children. Hoffman Declaration, pages 4-5.

[redacted]

Although the examiner considered several scientifically conservative statements regarding the acceptability of the animal model of record, such as, "this monkey model system has not been validated" (Hoffman declaration, page 6), and "[w]ith the exception of the work carried out in man, the validity of all the experimental systems is open to challenge" (Mitchell, page 2), we do not find that the examiner has reviewed the evidence of enablement provided by appellants as a whole.

The cases of In re Fouche, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971) and In re Brana, 51 F.3d 1560, 1563, 34 USPQ2d 1436, 1439 (Fed. Cir. 1995), recognize that 35 U.S.C. §101 rejections for utility present similar issues as 35 U.S.C. §112 rejections for nonenablement. Thus, it is appropriate to consider relevant utility case law to the present enablement issue.

In Brana, the Federal Circuit stated, "Our court's predecessor has determined that proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility." In re Brana, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995); In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961). In addition, "...pharmacological testing of animals is a screening procedure for testing new drugs for practical utility." Cross v. Iizuka, 753 F.2d 1040, 1051, 224 USPQ 739, 747 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1324, 1327, 206 USPQ 885, 890 (CCPA 1980).

[redacted]

It is appellants' position that successful in vivo testing for a particular pharmacological activity in an art accepted model (monkeys) establishes a significant probability that in vivo testing for this particular pharmacological activity will be successful in humans. On the facts before us, we agree.

Appellants submit that they have provided evidence of efficacy of the claimed formulation protective against Plasmodium vivax in the most reliable and standard animal model accepted by experts in the field for predicting the likelihood of success of the claimed invention in humans. Substitute Brief, page 13.

Based upon the relevant evidence as a whole, we find there to be a reasonable correlation between the disclosed in vivo utility and an in vivo activity in humans, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. Compare Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); Nelson v. Bowler, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980). Therefore, we will not sustain the rejection of the claims for lack of enablement.

Obviousness

Claims 1-3 stand rejected under 35 U.S.C. §103. As evidence of obviousness, the examiner cites McCutchan (1 and 2) and Harlow.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). A reference is considered in its entirety for what it fairly suggests to one skilled in the art. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

According to the examiner, McCutchan 1 and 2 describe monoclonal antibodies which are specific for epitopes of a peptide which corresponds to a region of the P. Vivax CS (circumsporozite) protein. The specification, page 2, states that the monoclonal antibody disclosed by McCutchan et al (Science 230) and McCutchan et al (U.S. Patent No. 4,693,994) is the monoclonal antibody of the instant invention which is designated NVS3. Answer, page 5. The examiner acknowledges that the McCutchan references do not teach a composition comprising a pharmaceutical amount of a monoclonal antibody NVS3 in a pharmaceutically acceptable carrier. Id.

Harlow is cited by the examiner as establishing that it was well known in the art at the time of the invention to produce solutions of monoclonal antibodies in phosphate

[redacted]

buffered saline (PBS) which is considered to be a pharmaceutically acceptable diluent for storage of antibodies.

The examiner summarizes (Answer, pages 5-6),

> It would have been obvious for one of ordinary skill in the art to produce solutions consisting of NVS3 monoclonal antibody as taught by McCutchan et al references. One of ordinary skill in the art would have been motivated to produce such compositions in order to form stable storage compositions, or working solutions for us in assays, etc. The antibody concentrations in such compositions would have been those which would be considered to be pharmaceutical amounts, and solutions comprising the NVS3 antibody PBS would be considered to be pharmaceutically injectable solutions given that the buffer PBS is a pharmaceutically acceptable diluent. Even though the appellants characterize the claimed formulations as being for use in passive protection against *P.vivax*, the claims read on the ingredients *per se*, which in the case of the instant claims are NVS3 antibody in a pharmaceutically acceptable carrier.

Appellants argue in response to this rejection that, at best the examiner has argued that it would be obvious to try using the NVS3 monoclonal antibody for passive immunization and that it would have some protective activity. Substitute Brief, page 24. Appellants argue the examiner has failed to provide evidence to support a reasonable expectation of the success of passive immunization using the monoclonal antibody, as claimed. Id. Furthermore, appellants argue that Harlow teaches away from the invention by recommending addition of sodium azide, a poison, as a preservative in monoclonal antibody solutions. Substitute Brief, page 32.

We agree with appellants that the examiner has failed to establish a prima facie case of obviousness on the record before us. McCutchan teaches the claimed monoclonal

antibody in the context of an analytical tool. Harlow, the secondary reference, states that when preparing a PBS solution of monoclonal antibodies in the laboratory, "[i]f there is no reason to avoid the use of sodium azide, add to 0.02%". Harlow, page 287. In our view, neither reference, however, provides any reason for one of ordinary skill in the art to avoid the use of sodium azide in preparing a monoclonal antibody solution, such as for preparing a composition for use in vivo.

The diagnostic use of a monoclonal antibody as described by McCutchan 1 and 2, in view of Harlow, would reasonably appear to have suggested that sodium azide be used in preparing such monoclonal antibody solutions. Therefore, taking the teachings of the references in their entirety, the references as a whole would have suggested to one of ordinary skill in the art a composition comprising a monoclonal antibody, PBS and sodium azide in an antibody solution, leading to a solution which is not a pharmaceutically acceptable formulation, as claimed. Moreover, we find no evidence of record suggesting the use of, or supporting a reasonable expectation of success for the use of the monoclonal antibody for preparation of a pharmaceutical formulation for passive immunization against P. vivax. Therefore, we will not sustain the rejection of the claims for obviousness.

CONCLUSION

The rejection of claims 1-3 under 35 U.S.C. §103 in view of McCutchan (1 and 2) and Harlow is reversed.

The rejection of claims 1-7, 11 and 12 under 35 U.S.C. §112, first paragraph is reversed.

[redacted]

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

Toni R. Scheiner Administrative Patent Judge	)
Demetra J. Mills Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Eric Grimes Administrative Patent Judge	)

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Polyakov, I. et al
Serial No.: 10/085,703
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Docket: 3/400-4-C4

Art Unit: 1645
Examiner: N. M. Minnifield

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Alexandria, VA 22313-1450

BRIEF ON APPEAL FROM THE PRIMARY EXAMINER'S DECISION TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Pursuant to the provisions of 35 U.S.C. § 134 and 37 C.F.R. § 1.191, applicants (hereinafter "appellants") respectfully appeal from the Primary Examiner's final rejection of all of the pending claims. A Notice of Appeal was timely filed on April 15, 2003. It is hereby requested that the time for filing this Appeal Brief be extended pursuant to 37 CFR 1.136(a) for two months, so that the extended period filing this Appeal Brief will end on August 15, 2003. Authorization is hereby given to charge the fee due under 37 C.F.R. § 1.17(c) to Deposit Account No. 02-2955, which is indicated by the enclosed Fee Transmittal Form (Form PTO/SB/17). If it is determined, however, that any additional fees under 37 C.F.R. §§ 1.16 or 1.17 are due in connection with this Appeal Brief, authorization is hereby given to charge such fees to Deposit Account No. 02-2955. This Appeal Brief is being filed in triplicate as required under 37 C.F.R. § 1.192(a).

REAL PARTY IN INTEREST

The real party in interest is Boehringer Ingelheim Vetmedica GmbH, Binger Str. 173, 55216 Ingelheim am Rhein, Germany.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any other currently pending appeal or interference that would directly affect, be affected by, or have a bearing on the Board's decision in the pending appeal.

STATUS OF CLAIMS

The instant application was filed with claims 1 and 2. Claims 1 and 2 are the subject of this appeal and set forth in the Appendix to this Appeal Brief.

STATUS OF AMENDMENTS

No amendments have been filed.

SUMMARY OF INVENTION

The instant claimed invention relates to two dermatomycosis vaccines comprising inactivated dermatophytes, wherein the inactivated dermatophytes **consist** of either eight or three specified dermatophyte strains, all of which were deposited according to the Budapest Treaty.

ISSUE PRESENTED FOR REVIEW

Whether claims 1 and 2 comply with 35 U.S.C. § 112, first paragraph.

GROUPING OF CLAIMS

Each of the two claims stand or fall independently as each claim provides different scope. Appellants therefore request that the Board independently consider the enablement of each claim in light of the arguments below.

ARGUMENT

Appellants respectfully maintain that claims 1 and 2 comply with 35 U.S.C. § 112, first paragraph, in all respects by enabling one of skill in the art to which the invention pertains to make and use the invention, as explained below. Unless indicated otherwise, all of the citations to "Office Action" below are references to the last Office Action dated February 5, 2003.

Copies of the cited Unpublished Board Opinions are enclosed for the Board's convenience. Such Unpublished Board Opinions are cited to show only the proper legal analysis and are acknowledged not to be binding precedent of the Board.

The Examiner rejected claims 1 and 2 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to

enable one of skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention (Office Action, page 2).

In response, appellants respectfully traverse the Examiner's rejection and maintain that the claims comply with 35 U.S.C. § 112, first paragraph, and all other statutory requirements in all respects.

In making this rejection, the Examiner has made many unsubstantiated allegations. Appellants will address each allegation made by the Examiner in order and explain why they are each either factually incorrect, legally irrelevant or improper, or both.

A. The Scope of the of Claims under Appeal

> "Where, as here, the issues presented for review concern the practical utility of the full scope of the subject matter claimed and the specification's capacity to enable one skilled in the art to make and use the full scope of the subject matter claimed, claim interpretation is a necessary prerequisite to resolution of the merits presented." (*In re Steele*, 134 U.S.P.Q. 292, 295 (CCPA 1962); *Ex parte Beck*, Appeal No. 94-3222, page 4 (UNPUBLISHED; Exhibit A); emphasis added).

Only the inventions defined by the claims need be explained in the patent application in a manner sufficient to be supported as required by 35 U.S.C. § 112, first paragraph (*Engel Industries, Inc. v. Lockformer Co.*, 20 U.S.P.Q.2d 1300, 1302 (Fed. Cir. 1991).

The claims as presented here for review each include the following clauses:

- "A dermatomycosis vaccine comprising inactivated dermatophytes": this clause indicates that the vaccine may, but does not necessarily have to comprise, in addition to the dermatophytes as specified *infra*, carriers, excipients, adjuvants etc. acceptable for and common in veterinary use as disclosed in the present specification.
- "wherein the inactivated dermatophytes **consist** of:" and listing by accession number either eight or three specified dermatophyte strains, each of which were deposited according to the Budapest Treaty. This part of the claim clearly points out that the

dermatophyte element of the vaccine as claimed is composed of only the deposited strains, see discussion *infra*.

The transitional phrase "consisting of" is close-ended and excludes any element, step, or ingredient not specified in the claim. See M.P.E.P. at § 2111.03; *In re Gray*, 11 U.S.P.Q. 255 (CCPA 1931); *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (Bd. App. 1948). When the phrase "consists of" appears in a clause of the body of a claim, rather than immediately following the preamble, it limits only the element set forth in that clause, other elements are not excluded from the claim as a whole. See M.P.E.P. § 2111.03; *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 230 U.S.P.Q. 45 (Fed. Cir. 1986).

Thus, claim 1 must be interpreted to include no less and no more than the following dermatophytes:

- *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277)
- *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279)
- *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278)
- *Trichophyton equinum* Strain No. VKPGF-929/381 (accession No. DSM 7276)
- *Microsporum canis* Strain No. VKPGF-928/1393 (accession No. DSM 7281)
- *Microsporum canis var. obesum* Strain No. VKPGF-727/1311 (accession No. DSM 7280)
- *Microsporum canis var. distortum* Strain No. VKPGF-728/120 (accession No. DSM 7275)
- *Microsporum gypseum* Strain No. VKPGF-729/59 (accession No. DSM 7274).

Similarly, claim 2 must be interpreted to include no less and no more than the following dermatophytes:

- *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277)
- *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279)
- *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278).

B. Appellants Have Taught How to Make the Vaccines within the Scope of the Claims

This fact is undisputed by the Examiner:

> "The Examiner agrees that the specification teaches how to make the claimed vaccine" (Office Action at page 3, last paragraph).

C. Appellants have Taught how to Use the Vaccines within the Scope of the Claims

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement". *In re Wright*, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993)(emphasis added). See also *In re Morehouse*, U.S.P.Q. 29, 32 (CCPA 1976); *Ex parte Charoenvit*, Appeal No. 1999-1413 (UNPUBLISHED; Exhibit B). The Examiner's conclusory statement "The rejection is maintained for the reasons of record" only accompanied by unsupported allegations not relating to the present claims does not satisfy this burden.

Upon careful review of the previous Office Action dated May 30, 2002, no proper explanation or sufficient reasons were given by the Examiner as to why the scope of protection provided by the claim is allegedly not enabled by the specification.

As no sufficient reasons can be found in either one of the Office Actions, the Office Actions regarding the parent application 09/256,915, to which benefit is claimed in the subject application, were reviewed. Quite surprisingly, the same examiner acknowledged the enablement for the use of the inactivated strain in a vaccine composition:

> "Claim 18, 21-23, 34 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for use of the inactivated strain**, does not reasonably provide enablement for one antigen from the dermatophytes, T. verrucosum, to be used in the vaccine composition." (Final Office Action dated August 29, 2003, page 3 at 6.; emphasis added)

Appellants fully agree with Examiner's conclusion that the specification is fully enabling for the use of any of the inactivated strains. Accordingly, if the use of a vaccine containing only one inactivated strain is considered to be disclosed in an enabling manner, how can the use of a vaccine containing eight or three of such strains not be considered to be disclosed in an enabling manner?

In short, if a vaccine comprising one strain is shown to provide immunity and to comply with the requirements of 35 U.S.C. 112, first paragraph, why should a vaccine comprising several of said strains not provide immunity?

The Examiner put forward several, unsupported allegations as discussed below:

(a) "It is not clear what Applicants used in the vaccine composition. Example 1, page 18 indicates that "[A]fter 2 days, 125 ml of each culture in suspension is taken and mixed in a single container. The vaccine may be prepared by mixing together various combinations of the given strains." Exactly what was the composition of the vaccine administered that gave the results found in Tables 9 and 10? It is not clear if all 8 dermatophytes were used or some combinations of 3, 4, 6 or 7 dermatophytes. It is not clear that the specific combination of 3 dermatophytes as set forth in claim 2 were used." (Office Action at page 2, 4. to page 3, first paragraph).

(b) "Specifically, the specification has not taught how to use the claimed vaccine. Mixing each culture in a single container or mixing together various combinations of the given cultures is set forth. However, it is not clear which composition (all 8 cultures in one container or various combinations of less than 8 cultures and if less than 8 cultures specifically which ones) was used to generate the data found on tables 9 and 10 of the specification." (Office Action at page 3, last paragraph to page 4, first paragraph).

(c) "Does Applicant intend for "immunogenic response" to mean that vaccine protection has been established, see page 11?" (Office Action at page 3, first paragraph). "Does the vaccine comprising a combination of cultures protect in the same manner as the individual cultures; is there a synergistic affect with regard to protection against ringworm infection?" The Examiner further cites Gudding et al (Can. Vet. J. 1995) and continues "Further, the inactivated vaccine against ringworm must be capable of eliciting both humoral and cellular immune responses, of which the cellular immune response is crucial for protection and adjuvants are important in stimulating the cellular branch of the immune system (pp. 303-304). In view of the state of the art it is not clear if protection has been established against ringworm infection when Applicants state (see tables 1-7) "establishes immunity". It is not clear what type of immunity is established. Applicant's vaccine composition does not recite a carrier or adjuvant, however Gudding indicates that the adjuvants are important in stimulating the cellular branch of the immune system and the cellular branch is crucial for protection.

Allegation (a)

With regard to allegation (a), the Examiner has cited only part of Example 1. Omitted is the preceding paragraph:

> "To produce 1 liter of vaccine, cultures are taken of the strains VKPGF-931/410, 930/1032, 929/381, 551/68, 928/1393, 727/1311, 728/120, and 729/59 and grown in agar/wort at 26°C for 15 days. Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer. The solution used is an aqueous solution containing 1% fermented hydrolyzed muscle protein, 10% glucose and 1% yeast extract. The concentration of microconidia is brought to 90 million per ml of homogenate. After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container." (emphasis added).

Therefore, from the quoted wording, it is clear to the skilled person that in cited Example 1 the 8-fold vaccine, exactly as claimed in claim 1, was prepared and used in prophylaxis and therapy.

The sentence "The vaccine may be prepared by mixing together various combinations of the given strains" (emphasis added), uses the term "may" which clearly indicates to the skilled person what optionally may be done, e.g. instead of eight claims, the combination of three strains as recited in claim 2 may be used in a vaccine according to the invention.

Allegation (b)

Regarding allegation (b), the wording of example 1 clearly states that each of the eight cultures is first cultured separately and homogenized:

> "Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer."

and then combined into one container:

> "After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container."

Further, the specification extensively describes immunizing the animals using the vaccine prepared in Example 1 to determine dosage to be given and the method of administration for prevention and treatment in ten different animal families (page 18, line 33 and Table 8). The effectiveness of the vaccine in preventing disease in 24 animal species is given (Example 2, page 21, and Table 9); and the effectiveness of the vaccine in treating infected animals in 18 different animal species is provided (Example 3, page 21 and Table 10).

Furthermore, clarification can also be drawn from page 3, lines 5-12 and 20-22 disclosing preferred vaccine combinations in the context of page 4, lines 8-18:

Page 3, lines 5-12:

> This aim has been achieved by using the following fungal strains as vaccinal strains: *Trichophyton verrucosum* (especially No. VKPGF-931/410), *Trichophyton mentagrophytes* (especially No. VKPGF-930/1032), *Trichophyton equinum* (especially No. VKPGF-929/381), *Trichophyton sarkisovii* (especially No. VKPGF-551/68), *Microsporum canis* (especially No. VKPGF-928/1393), *Microsporum canis var. obesum* (especially No. VKPGF-727/1311),

Microsporum canis var. distortum (especially No. VKPGF-728/120), *Microsporum gypseum* (especially No. VKPGF-729/59). Vaccines can be produced by using various combinations of antigenic material from the above strains together with a suitable carrier.

Page 3, lines 20-22:

"Another preferred combination of vaccine strains consists of *Trichophyton verrucosum* No. VKPGF-931/410, *Trichophyton mentagrophytes* No. VKPGF-930/1032, *Trichophyton sarkisovii* No. VKPGF-551/68, particularly for use in cattle."

Page 4, lines 8-18:

In order to prepare a vaccine the following procedure may be used, for example:

Cultures of the strains are homogenized in an aqueous solution containing 0.2 ti 2.0% fermented, hydrolyzed muscle protein (FGM-s), 5 to 12% glucose and 0.1 to 1.2% yeast extract. The concentration of the microconidia is adjusted to 40 to 120 million per milliliter and after 1 to 2 days the mixture is inactivated, *e.g.*, with thiomersal ($C_9H_9O_2SNaHg$) in the ration 1:10,000 to 1:25,000, or with another substance known from the prior art. The resulting suspension is packaged and is ready for use in animals.

The preparation of the vaccines, the dosage to be given and the method of administration for prevention and therapeutic treatment are explained in Examples 1 to 3.

With the before-mentioned extensive guidance provided to the skilled person, appellants have shown how to make and use both vaccines within the scope of the claims, including claim 2.

Furthermore, the Examiner did not consider and apply the factors and analysis of *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) and *Ex parte Forman*, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). In properly considering and applying the factors concerning enablement, the following factors should be considered: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

With regard to factors (1) and (2), to practice the invention, either 8 or 3 dermatophytes must be grown, mixed together in a single container, the mixture is inactivated, and the resulting vaccine is bottled (described in the specification on pages 4, lines 10-18, page 18, lines 15-31), and applied to animals at a dosage and with a route of administration as disclosed in Example 2, page 21, and Table 9 (prevention) as well as Example 3, page 21 and Table 10 (therapy). As set out *supra*, the dosage and route of administration is given for 10 different animal families, and guidance regarding efficacy of the 8-fold vaccine is given for 24 animal species (prevention) and 18 animal species (therapy) all of which represents a very limited amount of routine experimentation under a significant amount of guidance presented in the specification. If at all, there is minimal routine experimentation necessary to test the 3-fold vaccine in a similar manner as the 8-fold vaccine. With regard to factor (3), there are several in-depth working examples disclosing the preparation of vaccines according to the invention, the dosage, the route of preventive or therapeutic administration for numerous animal species. With regard to factors (4), (5), (6), and (7), as the nature of the invention is in the immunology, animal health and vaccine art, which is very highly developed, the state of the prior art is high, and the relative skill of those in the art is at a very high level, one would expect one of skill in the art would easily be able to use the directions in the specification to make and use the vaccines according to the invention. Regarding factor (8), it should be pointed out again that the claims presented for review are not generic claims, but are directed to two specific vaccines consisting of eight or three specified dermatophytes.

This situation is in contrast to that of *Ex parte Forman*, where the art was "undeveloped", that at the time (early 1980s) "experiments in genetic engineering produce, at best, unpredictable results", there were no apparent reproducible working examples presented outside the scope of the deposited microorganism strains, nor did there "appear to be ... a single detailed example that could be followed by another worker in another lab to obtain a single specific microorganism (vaccine) within appellants' claims, without recourse to the deposited strains recited in the allowed claims." *Ex parte Forman*, at 548. The instant situation is more like *In re Wands*, where enablement was shown, as appellants' disclosure, like Wands' disclosure, "provides considerable direction and guidance on how to practice their invention and presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known." *In re Wands* at 1406.

35 U.S.C. § 112, first paragraph, certainly does not require each and every embodiment of the invention to be exemplified. Even the lack of a working example (quite contrary to the situation here with several working examples), if all the other factors point to enablement, is not considered to render the invention non-enabled, if one skilled in the art will be able to practice it without an undue amount of experimentation (M.P.E.P. 2164.02; *In re Borkowski*, 164 U.S.P.Q. 642, 645 (CCPA 1970).

Further, the test is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue (M.P.E.P. § 2164.01; *In re Angstadt*, 190 U.S.P.Q. 214, 219 (CCPA 1976); *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, U.S.P.Q. 409, 413 (Fed. Cir. 1984).

The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *The Johns Hopkins University v. Cellpro Inc.* 47 U.S.P.Q.2d 1705, 1719; *PPG Indus., Inc. v. Guardian Indus. Corp.* 37 U.S.P.Q.2d 1618, 1623 (emphasis added).

With the significant amount of guidance presented in the specification, the minimal routine experimentation necessary to test the 3-fold vaccine in a similar manner as the 8-fold vaccine can certainly not be considered undue.

Allegation (c)

With regard to allegation (c), appellants cite Taber's cyclopedic medical dictionary, in existence since 1940 and clearly the standard to the skilled person (Exhibit C). It is appropriate to compare the meaning of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. *In re Barr*, 170 U.S.P.Q. 330 (CCPA 1971).

"Vaccine" is defined to be used as follows:

> "FUNCTION: Vaccines are used to stimulate **an immune response** in the body by creating antibodies **or** activated T lymphocytes capable of controlling the organism. **The result is protection against disease**; the duration depends on the particular vaccine. (emphasis added)"

Therefore, for the use of a vaccine to be enabled, it is fully sufficient to stimulate an immune response which can either be the generation of antibodies or activated T lymphocytes, both requirements do not need to be satisfied. The Examiner's arbitrary requirement of requiring both humoral (antibody-mediated) and cellular (T lymphocyte) responses is neither scientifically justified nor founded in the law. To fulfil the requirements of 35 U.S.C. § 112, first paragraph, it is fully sufficent that the vaccines according to the invention provide an immune response. This is extensively exemplified in Examples 2 and 3, page 21, and Tables 9 and 10 of the specification.

Likewise, the Examiner's arbitrary requirement for an adjuvant to be present in the vaccine is neither scientifically justified nor founded in the law as discussed *infra*. Appellants successfully sell Insol® Dermatophyton and Insol® Trichophyton, wherein the dermatophytes consist of the strains as claimed in claim 1 and 2 presented for review (package inserts presented in Exhibits D and E, respectively). Both vaccines do not require adjuvants due to the superior properties of the vaccine strains contained therein. Thus, it is again respectfully submitted that the subject matter claimed fully complies with the requirements set forth in 35 U.S.C. § 112, first paragraph.

In many of these allegations, the Examiner seems to be attempting to shift the burden to the appellants to affirmatively prove that appellants are entitled to a patent, when it is the Examiner's burden to prove that appellants are not entitled to a patent with rejections that are supported by evidence and a rational basis. This the Examiner has not done.

Appellants contend that the legal standard is whether a claim is understandable to one of ordinary skill in the art and that it defines subject matter that appellants regard as the invention. Federal Circuit cases have made clear that claim language must not be analyzed in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings in the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *In re Marosi*, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 221 U.S.P.Q. 1 (Fed.Cir.1983); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 220 U.S.P.Q. 303 (Fed.Cir.1983).

In conclusion, appellants have shown by description and examples how to produce the vaccines according to the invention, and also how to use the vaccines for prophylaxis and therapy in numerous animal species. Accordingly, appellants have shown how to make and use both vaccines within the scope of the claims.

Accordingly, appellants submit that, based on the arguments above, claims 1 and 2, comply with 35 U.S.C. § 112, first paragraph, as well as with all other statutory requirements of the U.S. Patent Law. An applicant who complies with the statutory requirements is entitled to a patent. *In re Rouffet*, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998); *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992); *In re Grabiak*, 226 U.S.P.Q. 870, 873 (Fed. Cir. 1985); *In re Rinehart*, 189 U.S.P.Q. 143, 147 (C.C.P.A. 1976).

Consequently, appellants respectfully maintain that the Examiner's rejections of pending claims 1 and 2 were improper, and request that the Board reverse all of the appealed rejections and direct the Examiner to issue a Notice of Allowance for all of the pending claims.

APPENDIX

The following claims 1 and 2 are on appeal.

1. A dermatomycosis vaccine comprising inactivated dermatophytes, wherein the inactivated dermatophytes consist of: *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277), *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279), *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278), *Trichophyton equinum* Strain No. VKPGF-929/381 (accession No. DSM 7276), *Microsporum canis* Strain No. VKPGF-928/1393 (accession No. DSM 7281), *Microsporum canis var. obesum* Strain No. VKPGF-727/1311 (accession No. DSM 7280), *Microsporum canis var. distortum* Strain No. VKPGF-728/120 (accession No. DSM 7275), and *Microsporum gypseum* Strain No. VKPGF-729/59 (accession No. DSM 7274).

2. A dermatomycosis vaccine comprising inactivated dermatophytes, wherein the inactivated dermatophytes consist of: *Trichophyton verrucosum* Strain No. VKPGF-931/410 (accession No. DSM 7277), *Trichophyton mentagrophytes* Strain No. VKPGF-930/1032 (accession No. DSM 7279), and *Trichophyton sarkisovii* Strain No. VKPGF-551/68 (accession No. DSM 7278).

Certificate of Mailing Under 37 C.F.R. § 1.8(a)
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA 22313-1450, on August 15, 2003.

Susan K. Pocchiari

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August 15, 2003

Dated

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THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 30

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LEE R. BECK and RALPH J. STOLLE

Appeal No. 94-3222
Application 07/815,630[1]

HEARING: July 16, 1998

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[1] Application for patent filed December 30, 1991. According to applicants, this application is a continuation of Application 07/548,419, filed July 5, 1990, now abandoned; which is (1) a continuation-in-part of Application 07/431,639, filed November 6, 1989, now U.S. 5,130,128, issued July 14, 1992; and (2) a continuation-in-part of Application 07/177,223, filed April 4, 1988, now U.S. 4,956,349, issued September 11, 1990. Application 07/431,639 is a continuation-in-part of Application 07/161,039, filed February 26, 1988, now U.S. 4,879,110, issued November 7, 1989. Both Applications 07/161,039 and 07/177,223 are continuations-in-part of Application 07/001,848, filed January 9, 1987, now U.S. 4,897,265, issued January 30, 1990; which is a divisional of Application 06/546,162, filed October 27, 1983, now U.S. 4,636,384, issued October 23, 1990; which is a continuation-in-part of Application 06/384,625, filed June 3, 1982, now abandoned. U.S. 4,636,384 was reissued as U.S. Re. 33,403 on October 23, 1990.

Before WINTERS, WILLIAM F. SMITH, and GRON, Administrative Patent Judges.

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

This is an appeal under 35 U.S.C. § 134 from an examiner's final rejection of Claims 2 and 6-9.

On consideration of the record of this case in its entirety, it is hereby ORDERED that

the examiner's final rejections in this case are VACATED, and that

this application is REMANDED to the examiner for further action consistent with the following opinion.

1. Introduction

Claims 1-9 are pending in this application. In accordance with 37 CFR § 1.142(b), Claims 1 and 3-5 have been withdrawn from further consideration by the examiner as directed to non-elected subject matter under a restriction requirement. Claims 2 and 6-9 stand rejected as unpatentable under 35 U.S.C. § 101 purportedly as drawn to subject matter without practical utility and under

35 U.S.C. § 112, first paragraph, as supported by a specification which purportedly would not have enabled persons skilled in the art to use the full scope of products and methods claimed for the utility indicated.

According to appellants, Claims 2 and 6-9 stand or fall together (Brief on Appeal, p. 4). Claims 2 and 6 represent the subject matter claimed and read:

> 2. A food product comprising a composition wherein said composition comprises a non-antibody fraction of milk and wherein said non-antibody fraction of milk ameliorates, in a subject with an allergy to an allergen, the symptoms of said allergy of said subject to said allergen when said fraction is ingested by said subject and wherein said fraction is produced by the process comprising:
>
> (a) administering said allergy to a milk-producing animal;
>
> (b) collecting the milk from said animal of part (a);
>
> (c) filtering the milk of part (b) through a filter which excludes molecules of greater than 100,000 daltons; and
>
> (d) collecting the effluent from the filtration of part (c) wherein said effluent contains said fraction.
>
> 6. A method for desensitizing a subject to an allergen wherein said method comprises orally administering to said subject a food product, in an amount and for a time sufficient to produce an amelioration in said subject of

symptoms of allergy to said allergen, wherein said food product comprises a non-antibody fraction of milk from a milk-producing animal that has been immunized with said allergen.

2. Discussion

It should have been apparent from the questions this panel of the Board asked counsel at Oral Hearing on July 16, 1998, that we should not rule on the merits of this appeal because, as a matter of law, it would be incorrect to do so. Accordingly, we vacate the examiner's decision finally rejecting the subject matter on appeal under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, for reasons which follow.

We have searched the record of this case and do not find any indication that the metes and bounds of the subject matter claimed have been established. Where, as here, the issues presented for our review concern the practical utility of the full scope of the subject matter claimed and the specification's capacity to enable one skilled in the art to make and use the full scope of the subject matter claimed, claim interpretation is a necessary prerequisite to resolution of the merits of the issues presented. See In re Steele, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962)(When an analysis

of the claims leaves the reviewing body in a quandary as to what they cover, the examiner and the Board may not rely on speculation as to the meaning of the claims in support of a rejection.) In re Moore, 439 F.2d 1232, 169 USPQ 236 (CCPA 1971) instructs at 1235, 169 USPQ at 238 [footnotes omitted]:

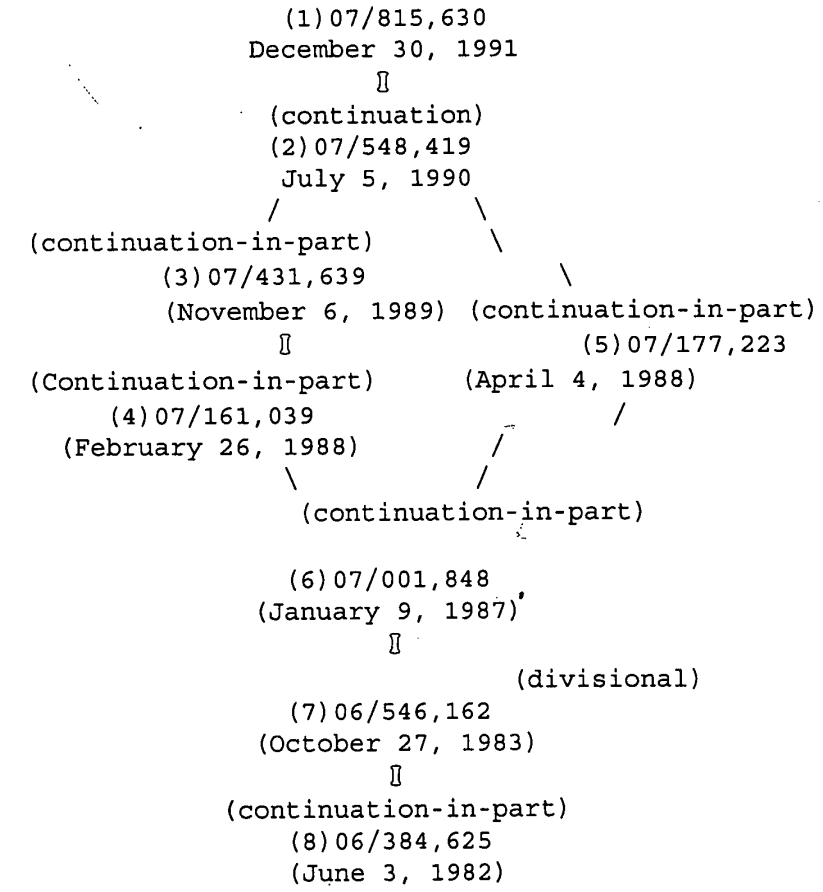
> [The] . . . first inquiry therefore is merely to determine whether the claims do . . . set out and circumscribe a particular area with a reasonable degree of precision and particularity. It is here where the definiteness of the language employed must be analyzed--not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.
>
> Once having determined that the subject matter defined by the claims is particular and definite, the analysis then turns to the first paragraph of section 112 to determine whether the scope of protection sought is supported and justified by the specification disclosure.

For example, the examiner appears not to have interpreted the term "allergen" in Claims 2 and 6, the phrases "allergy to an allergen" in Claim 2 and "allergy to said allergen" in Claim 6, the phrases "ameliorates . . . the symptoms of said allergy" in Claim 2 and "an amelioration . . . of symptoms of allergy" in Claim 6, the term "non-antibody fraction" in Claims 2 and 6, the phrase "a non-antibody fraction of milk from a milk-producing animal that has been immunized with said

allergen" in Claim 6 (emphasis added), and the phrase "excludes molecules of greater than 100,000 daltons" in Claim 2. We will refrain from considering the patentability of the claimed subject matter under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, until the examiner has first interpreted the meaning and breadth of the aforementioned terms and phrases in light of the description of the claimed subject matter in the specification and the teachings of the prior art. Id. at 1235, 169 USPQ at 238.

Moreover, we do not understand how it is possible for the examiner of this application to consider the meaning and breadth of the terms and phrases in appellants' claims in light of the prior art or to determine whether this specification would have enabled persons skilled in the art at the pertinent time to make and use the full scope of invention claimed without having first determined the effective filing date of the subject matter claimed. Unless and until the effective filing date of the subject matter presently claimed is established, what is and what is not prior art as to the subject matter presently claimed can be no more than speculative.

For example, applicants claim the benefit of priority under 35 U.S.C. § 120 through two lineages (Spec., p. 1, first para.):



With those two lines in mind, we list the following information:

(1) Application 07/815,630 for "IMMUNE SUPPRESSIVE PRODUCT," was filed December 30, 1991, in the names of Beck and Stolle.

(2) Application 07/548,419 was filed July 5, 1990, also in the names of Beck and Stolle and is said to be the parent of continuation Application 07/815,630 (this application);

(3) Application 07/431,639 for "USE OF HONEY AS VACCINE" was filed November 6, 1989, in the sole name of Stolle and issued July 14, 1992, as U.S. 5,130,128;

(4) Application 07/161,039 for "ANTIHYPERTENSIVE HYPERIMMUNE MILK, PRODUCTION, COMPOSITION, AND USE" was filed February 26, 1988, in the names of Beck and Stolle and issued November 7, 1989, as U.S. 4,879,110;

(5) Application 07/177,223 for "ANTI-INFLAMMATORY FACTOR, METHOD OF ISOLATION, AND USE" was filed April 4, 1988, in the sole name of Beck and issued September 11, 1990, as U.S. 4,956,349;

(6) Application 07/001,848 for "METHOD FOR TREATING DISORDERS OF THE VASCULAR AND PULMONARY SYSTEMS" was filed January 9, 1987, in the names of Stolle and Beck and issued January 30, 1990, as U.S. 4,897,265;

(7) Application 07/546,162 for "METHOD FOR TREATING DISORDERS OF THE VASCULAR AND PULMONARY SYSTEMS" was filed October 27, 1983, in the names of Stolle and Beck and issued January 13, 1987, as U.S. 4,636,384; and

(8) Application 07/384,625, now abandoned, was filed June 3, 1982, in the names of Stolle and Beck.

We note from the above listing that while the subject matter appellants claim appears to be entitled to the July 5, 1990, filing date of (2) Application 07/548,419 filed in the names of Beck and Stolle as a file-wrapper continuation of this application, it is not at all apparent that the full scope of the subject matter presently claimed is entitled either to the November 6, 1989, filing date of (3) Application 07/431,639 for "USE OF HONEY AS VACCINE" filed in the sole name of Stolle or the April 4, 1988, filing date or (5) Application 07/177,223 for "ANTI-INFLAMMATORY FACTOR, METHOD OF ISOLATION, AND USE" filed in the sole name of Beck. In fact, this record is noticeably devoid of any indication that the effective filing date of the subject matter claimed has been determined. Accordingly, it is our view that claim interpretation in light of the prior art cannot have been adequately done without first determining the merits of

applicants' claims under 35 U.S.C. § 120 so as to enable one to establish what constitutes the prior art under 35 U.S.C. § 102.

Moreover, while compliance with the requirements of 35 U.S.C. § 112, first paragraph, is normally determined as of the filing date of the pending application, the examiner, when faced with an intervening reference, may be required to focus on the filing date of a prior application as the result of the applicants' claims for priority under 35 U.S.C. § 120. United States Steel Corp. v. Phillips Petroleum Co., 865 F.2d 1247, 1251, 9 USPQ2d 1461, 1464 (Fed. Cir. 1989). We appear to have just such a case before us.

On their face, Stolle, U.S. 5,130,128, filed November 6, 1989, and Beck, U.S. 4,956,349, filed April 4, 1988, appear to be prior art under 35 U.S.C. § 102(e) whether or not they are commonly assigned with this application filed in the names of Beck and Stolle. See In re Bartfeld, 925 F.2d 1450, 17 USPQ2d 1885 (Fed. Cir. 1991). Moreover, Stolle and Beck, U.S. 4,636,384 and U.S. 4,732,757 may be prior art under 35 U.S.C. § 102(b). Accordingly, faced with what prima facie appears at least in part to be prior art of record and applicants' claims for priority under 35 U.S.C. § 120 in this case, the examiner

should determine the effective filing date of the subject matter here claimed before ruling on patentability under either 35 U.S.C. § 112, first paragraph, § 101, § 102, or § 103. It is as of the effective filing date that compliance with 35 U.S.C. §§ 112, first paragraph, and 101 and prior art availability must be determined.

Only after determining the effective filing date of the subject matter claimed may the examiner (1) determine whether appellants' claims satisfy 35 U.S.C. § 112, second paragraph, in light of applicants' disclosure and the prior art, (2) consider whether the subject matter claimed is patentable under 35 U.S.C. § 101 or whether applicants' disclosure would have enabled one skilled in the art to make and use the full scope of the claimed subject matter as required by 35 U.S.C. § 112, first paragraph, (3) determine patentability under 35 U.S.C. §§ 102 and 103 in view of the prior art (compare Chester v. Miller, 906 F.2d 1574, 1576, 15 USPQ2d 1333, 1336 (Fed. Cir. 1990), citing In re Gosteli, 872 F.2d 1008, 1010-1011, 10 USPQ2d 1614, 1616 (Fed. Cir. 1989)), and (4) determine whether the subject matter claimed in this case is unpatentable for obviousness-type

double-patenting of subject matter claimed in any one or more of the U.S. patents which have issued from applications for which

priority under 35 U.S.C. § 120 here is claimed.[2]

We will allow the examiner of this case to determine in the first instance the effective filing date of the subject matter claimed, the scope and content of the pertinent prior art, compliance with the requirements of the second paragraph of Section 112, compliance with Section 101 and the first paragraph of Section 112, and patentability of the claimed subject matter under 35 U.S.C. § 102, under 35 U.S.C. § 103, and over subject matter claimed in commonly assigned patents absent the filing of effective terminal disclaimers. For this panel to review the merits of the examiner's decision rejecting the claims on appeal under 35 U.S.C. § 101 and under 35 U.S.C. § 112, first paragraph, at this time without those preliminary determinations having been made by an examiner is

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[2] The examiner may wish to consider obviousness-type double-patenting issues. However, take note that if questions of obviousness-type double patenting of subject matter claimed in issued patents come to light, the examiner may want to consider whether adhering to unpatentability determinations under 35 U.S.C. § 101 or 112, first paragraph, for lack of utility is consistent with the presumption of validity of the patented subject matter.

inconsistent with our review function. See 35 U.S.C. § 7 ("The Board . . . shall . . . review adverse decisions of examiners . . . .") Accordingly, we vacate the examiner's final rejections and remand the case to the examining corps for action consistent with this opinion.

This application, by virtue of its "special" status, requires an immediate action, M.P.E.P. § 708.01(d). It is important that the Board be informed promptly of any action affecting the appeal in this case.

VACATED and REMANDED

SHERMAN D. WINTERS Administrative Patent Judge)	)	
WILLIAM F. SMITH Administrative Patent Judge)	)	BOARD OF PATENT APPEALS AND INTERFERENCES
TEDDY S. GRON	)	

Administrative Patent Judge)

Appeal No. 94-3222
Application 07/815,630

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The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte YUPIN CHAROENVIT, STEPHEN L. HOFFMAN,
RICHARD L. BEAUDOIN, DECEASED, BY BARBARA A. BEAUDOIN

Appeal No. 1999-1413
Application No. 08/176,024

ON BRIEF

Before SCHEINER, MILLS and GRIMES, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

[redacted]

This is a decision on appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 7, 11, and 12, which are all of the claims pending in the application.

Claims 1, 4, and 11 are representative and read as follows:

1. A formulation protective against Plasmodium vivax for a time commensurate with the time monoclonal antibody Navy Vivax Sporozoite 3 (HB10615) remains at pharmacologically active levels in a subject's blood stream, comprising a pharmaceutical amount sufficient to provide passive immunization of Navy Vivax Sporozoite 3 (HB10615) in a pharmaceutically suitable injectable solution.

4. A method of providing protection from Plasmodium vivax induced malaria for subjects experiencing exposure to infected mosquitoes, for a time commensurate with the time monoclonal antibody Navy Vivax Sporozoite 3 (HB 10615) remains at pharmacologically active levels in a subject's blood stream, that comprises introducing and circulating the antibody Navy Vivax Sporozoite 3 (HB 10615) in the subject's blood stream.

11. A humanized antibody capable of providing passive protection against Plasmodium vivax wherein said antibody has a variable region comprising the hyper variable regions of the heavy and light chains of monoclonal antibody Navy Sporozoite 3 (HB10615) and human antibody framework regions.

The examiner relies on the following references:

McCutchan et al (McCutchan 1) 4,694,944 Sept. 15, 1987

McCutchan, T.F. et al (McCutchan 2). "Sequence of the Immunodominant Epitope for the Surface Protein Sporozoites of Plasmodium vivax," Science, Vol. 23, pp. 1381-1383 (1985)

Harlow et al. (Harlow), Antibodies, A Laboratory Manual, Cold Spring Harbor Laboratory pp. 287 (1988)

Charoenvit, Y. et al. (Charoenvit), "Inability of Malaria Vaccine to Induce Antibodies to a Protective Epitope Within its Sequence," Science, Vol. 251, pp. 668-671 (1991)

Harris et al. (Harris), "Therapeutic Antibodies - The Coming of Age," Tibtech, Vol. 11, pp. 42-44 (1993)

Mitchell, G. H., (Mitchell), "An Update on Candidate Malaria Vaccines," Parasitology, Vol. 98, New York, pp. S29-S46 (1989)

Grounds of Rejection

1. Claims 1-3 stand rejected under 35 U.S.C. §103. As evidence of obviousness, the examiner cites McCutchan (1 and 2) and Harlow.

2. Claims 1-7, 11 and 12 stand rejected under 35 U.S.C. §112, first paragraph. As evidence of nonenablement, the examiner cites Charoenvit, Harris, and Mitchell.

We reverse both rejections.

DISCUSSION

Procedural Matters

In this case, an Appeal Brief with four attached 1.132 declarations was filed concurrent with a proposed amendment, on March 1, 1996. After several interviews and written communications, amended claims were entered by the Examiner, the effect of amendment entry on the rejections of record was communicated to the appellant on August 21, 1996, and a Substitute Brief was filed September 20, 1996, containing arguments directed to the amended claims. The Substitute Brief also refers to the

declarations by Drs. Steven L. Hoffman (1st and 2nd declarations), Yupin Charoenvit, and Thomas F. McCutchan, which were attached to the original Brief.

In the Examiner's Answer, four rejections under 35 U.S.C. § 103 were withdrawn. No new grounds of rejection were made, and no Reply Brief was filed.

Background

Plasmodium vivax is one of the four species of parasite causing malaria in humans (specification, page 1). Despite major efforts over at least 20 years, a commercially viable malaria vaccine has not been achieved (page 2 of the December 28, 1993 amendment to the specification). The present invention involves a monoclonal antibody, here designated NVS3. The monoclonal antibody has been described in the prior art (specification, page 2). This antibody binds to an epitope within a repeated nine amino acid sequence of the circumsporozoite protein of P. vivax (specification, page 8). Prior to the invention, recombinant proteins comprising the P. vivax repeated amino acid sequence failed to induce a significant protective effect in Saimiri monkeys in active immunization experiments (specification, pages 3-4). An object of this invention is to provide passive protection against P. vivax by administering the antibody to a subject, where the antibodies

bind to P. vivax sporozoites in the circulation of the host and render the sporozoites noninfectious thereby preventing malarial disease (specification, pages 4 and 7-8).

Enablement

Claims 1-7, 11 and 12 stand rejected under 35 U.S.C. §112, first paragraph. As evidence of nonenablement, the examiner cites Charoenvit, Harris, and Mitchell.

Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." In re Wands, 858 F.2d 73, 736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (the first paragraph of section 112 requires that the scope of protection sought in a claim bear a reasonable correlation to the scope of enablement provided by the specification). Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971).

An analysis of whether the claims under appeal are supported by an enabling disclosure requires a determination of whether that disclosure contained sufficient information regarding the subject matter of the appealed claims as to enable one skilled in the pertinent art to make and use the claimed invention. In order to establish a prima facie

case of lack of enablement, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. See In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). See also In re Morehouse, 545 F2d 162, 165, 192 USPQ 29, 32 (CCPA 1976). The threshold step in resolving this issue is to determine whether the examiner has met his burden of proof by advancing acceptable reasoning inconsistent with enablement.

Factors to be considered by the examiner in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman, [230 USPQ 546, 547 (Bd Pat App Int 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In the present case, the examiner cites the state of the art and the lack of working examples involving humans as the factors leading to a conclusion of non-enablement. Specifically, the examiner argues (Answer, page 6):

> The state of the art to which the invention pertains is such that as of this date passive immunization has not been used to prevent malaria in humans and that there are no vaccines for active or passive immunization that are accepted as being effective for prevention of P. vivax malaria. Charoenvit et al. (Science 251) states that it has never been definitively established in humans that circulating antibodies to the sporozoite of Plasmodium can prevent infection. Furthermore, Harris et al. establishes the use of monoclonal antibodies for in vivo human therapy is art-recognized to be highly experimental and unpredictable to those of skill in the art. The record contains no working examples relating to the use of the NVS3 antibody for treatment of P. vivax malaria in humans....
>
> The invention has been exemplified using the monkey model. However, the evidence obtained using the monkey model is not sufficient to allow one of ordinary skill in the art to predict the ability to practice the claimed invention for treatment of humans given that the monkey model used to exemplify the claimed invention is not an art-accepted model which is recognized as having a clear correlation with human efficacy for the evaluation of agents for passive immunotherapy of malaria.

On the other hand, the appellants argue that proof of efficacy in humans is not required, and that the monkey animal model tests disclosed in the specification are accepted by experts in the field. Substitute Brief, pages 13-15.

The specification provides a working example demonstrating efficacy of the claimed formulation in a nonhuman primate, the Saimiri monkey. Example 3, pages 13-15. In addition, the Hoffman Declaration of record provides an expert opinion that "most experts in the field consider this monkey model to be the most reliable system for predicting what will occur in humans." Hoffman Declaration, page 6. The Hoffman Declaration also cites long-held knowledge in the art of passive immunotherapy for acute malaria in human children. Hoffman Declaration, pages 4-5.

[redacted]

Although the examiner considered several scientifically conservative statements regarding the acceptability of the animal model of record, such as, "this monkey model system has not been validated" (Hoffman declaration, page 6), and "[w]ith the exception of the work carried out in man, the validity of all the experimental systems is open to challenge" (Mitchell, page 2), we do not find that the examiner has reviewed the evidence of enablement provided by appellants as a whole.

The cases of In re Fouche, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971) and In re Brana, 51 F.3d 1560, 1563, 34 USPQ2d 1436, 1439 (Fed. Cir. 1995), recognize that 35 U.S.C. §101 rejections for utility present similar issues as 35 U.S.C. §112 rejections for nonenablement. Thus, it is appropriate to consider relevant utility case law to the present enablement issue.

In Brana, the Federal Circuit stated, "Our court's predecessor has determined that proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility." In re Brana, 51 F.3d 1560, 1567, 34 USPQ2d 1436, 1442 (Fed. Cir. 1995); In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219 (CCPA 1961). In addition, "...pharmacological testing of animals is a screening procedure for testing new drugs for practical utility." Cross v. Iizuka, 753 F.2d 1040, 1051, 224 USPQ 739, 747 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1324, 1327, 206 USPQ 885, 890 (CCPA 1980).

It is appellants' position that successful in vivo testing for a particular pharmacological activity in an art accepted model (monkeys) establishes a significant probability that in vivo testing for this particular pharmacological activity will be successful in humans. On the facts before us, we agree.

Appellants submit that they have provided evidence of efficacy of the claimed formulation protective against Plasmodium vivax in the most reliable and standard animal model accepted by experts in the field for predicting the likelihood of success of the claimed invention in humans. Substitute Brief, page 13.

Based upon the relevant evidence as a whole, we find there to be a reasonable correlation between the disclosed in vivo utility and an in vivo activity in humans, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. Compare Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); Nelson v. Bowler, 626 F.2d 853, 856, 206 USPQ 881 (CCPA 1980). Therefore, we will not sustain the rejection of the claims for lack of enablement.

Obviousness

Claims 1-3 stand rejected under 35 U.S.C. §103. As evidence of obviousness, the examiner cites McCutchan (1 and 2) and Harlow.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). A reference is considered in its entirety for what it fairly suggests to one skilled in the art. In re Wesslau, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). With this as background, we analyze the prior art applied by the examiner in the rejection of the claims on appeal.

According to the examiner, McCutchan 1 and 2 describe monoclonal antibodies which are specific for epitopes of a peptide which corresponds to a region of the P. Vivax CS (circumsporozite) protein. The specification, page 2, states that the monoclonal antibody disclosed by McCutchan et al (Science 230) and McCutchan et al (U.S. Patent No. 4,693,994) is the monoclonal antibody of the instant invention which is designated NVS3. Answer, page 5. The examiner acknowledges that the McCutchan references do not teach a composition comprising a pharmaceutical amount of a monoclonal antibody NVS3 in a pharmaceutically acceptable carrier. Id.

Harlow is cited by the examiner as establishing that it was well known in the art at the time of the invention to produce solutions of monoclonal antibodies in phosphate

buffered saline (PBS) which is considered to be a pharmaceutically acceptable diluent for storage of antibodies.

The examiner summarizes (Answer, pages 5-6),

> It would have been obvious for one of ordinary skill in the art to produce solutions consisting of NVS3 monoclonal antibody as taught by McCutchan et al references. One of ordinary skill in the art would have been motivated to produce such compositions in order to form stable storage compositions, or working solutions for us in assays, etc. The antibody concentrations in such compositions would have been those which would be considered to be pharmaceutical amounts, and solutions comprising the NVS3 antibody PBS would be considered to be pharmaceutically injectable solutions given that the buffer PBS is a pharmaceutically acceptable diluent. Even though the appellants characterize the claimed formulations as being for use in passive protection against *P.vivax*, the claims read on the ingredients *per se*, which in the case of the instant claims are NVS3 antibody in a pharmaceutically acceptable carrier.

Appellants argue in response to this rejection that, at best the examiner has argued that it would be obvious to try using the NVS3 monoclonal antibody for passive immunization and that it would have some protective activity. Substitute Brief, page 24. Appellants argue the examiner has failed to provide evidence to support a reasonable expectation of the success of passive immunization using the monoclonal antibody, as claimed. Id. Furthermore, appellants argue that Harlow teaches away from the invention by recommending addition of sodium azide, a poison, as a preservative in monoclonal antibody solutions. Substitute Brief, page 32.

We agree with appellants that the examiner has failed to establish a prima facie case of obviousness on the record before us. McCutchan teaches the claimed monoclonal

antibody in the context of an analytical tool. Harlow, the secondary reference, states that when preparing a PBS solution of monoclonal antibodies in the laboratory, "[i]f there is no reason to avoid the use of sodium azide, add to 0.02%". Harlow, page 287. In our view, neither reference, however, provides any reason for one of ordinary skill in the art to avoid the use of sodium azide in preparing a monoclonal antibody solution, such as for preparing a composition for use in vivo.

The diagnostic use of a monoclonal antibody as described by McCutchan 1 and 2, in view of Harlow, would reasonably appear to have suggested that sodium azide be used in preparing such monoclonal antibody solutions. Therefore, taking the teachings of the references in their entirety, the references as a whole would have suggested to one of ordinary skill in the art a composition comprising a monoclonal antibody, PBS and sodium azide in an antibody solution, leading to a solution which is not a pharmaceutically acceptable formulation, as claimed. Moreover, we find no evidence of record suggesting the use of, or supporting a reasonable expectation of success for the use of the monoclonal antibody for preparation of a pharmaceutical formulation for passive immunization against P. vivax. Therefore, we will not sustain the rejection of the claims for obviousness.

CONCLUSION

The rejection of claims 1-3 under 35 U.S.C. §103 in view of McCutchan (1 and 2) and Harlow is reversed.

The rejection of claims 1-7, 11 and 12 under 35 U.S.C. §112, first paragraph is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

REVERSED

Toni R. Scheiner Administrative Patent Judge	)
Demetra J. Mills Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND) INTERFERENCES
Eric Grimes Administrative Patent Judge	)

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V 1. *Vibrio; vision; visual acuity.* **2.** Symbol for the element vanadium.

V̇ 1. Symbol for gas flow. **2.** Symbol for ventilation.

v L. *vena,* vein; *volt.*

vaccina (văk-sī'nă) Vaccinia.

vaccinable (văk-sĭn'ă-b'l) Capable of being successfully vaccinated.

vaccinal (văk'sĭn-ăl) Rel. to vaccine or to vaccination.

vaccinate (văk'sĭn-āt) [L. *vaccinus,* pert. to cows] To inoculate with vaccine to produce immunity against disease.

vaccination (văk"sĭ-nā'shŭn) [L. *vaccinus,* pert. to cows] **1.** Inoculation with any vaccine or toxoid to establish resistance to a specific infectious disease. SEE: *immunization.* **2.** A scar left on the skin by inoculation of a vaccine.

vaccine (văk'sēn, văk-sēn') [L. *vaccinus,* pert. to cows] A suspension of infectious agents, or some part of them, given for the purpose of establishing resistance to an infectious disease. SEE: table.

Vaccines comprise four general classes:

1. Those containing living attenuated infectious organisms, such as vaccine for poliomyelitis.
2. Those containing infectious agents killed by physical or chemical means, such as vaccines used to protect human beings against typhoid fever, rabies, and whooping cough.
3. Those containing soluble toxins of microorganisms, sometimes used as such, but generally forming toxoids, such as the one used in the prevention of diphtheria and tetanus.
4. Those containing substances extracted from infectious agents, such as capsular polysaccharides extracted from pneumococci.

FUNCTION: Vaccines are used to stimulate an immune response in the body by creating antibodies or activated T lymphocytes capable of controlling the organism. The result is protection against a disease; the duration depends on the particular vaccine. Recovery from measles or diphtheria, for example, usually provides lifelong immunity. The immune system has produced antibodies and memory cells for these pathogens so that subsequent exposure does not result in disease. A successful vaccine does the same thing, usually without risk of illness. The measles vaccine is believed to provide lifelong immunity, but the diphtheria vaccine requires periodic booster doses. More than one type of vaccine may be available for immunization against a specific infectious agent. SEE: *diphtheria; immune response; immunity; immunization; immunobiologics.*

autogenous v. Bacterial vaccine pared from lesions of the individual inoculated. SYN: *homologous v.*

bacterial v. A suspension of killed tenuated bacteria; used for injection the body to induce development of a immunity to the same organism.

BCG v. Bacille Calmette-Guéri preparation of a dried, living cultu *Mycobacterium tuberculosis.* In with a high incidence of tuberculosis used in prophylactic vaccination fants against tuberculosis. It is also in adults who are at high and unavoi risk of becoming infected with tube sis. A disadvantage of use of this va is that it produces hypersensitivity berculin. As a result, the skin test f berculin sensitivity becomes positive may persist for 5 years. There is no to distinguish a positive skin test d BCG from one caused by infection *Mycobacterium tuberculosis.*

cholera v. A vaccine prepared killed *Vibrio cholerae.* It is effectiv only a few months.

diphtheria v. SEE: *DPT v.*

DPT v. A combination of diphtheri tetanus toxoids and killed pertussi cilli that is administered intramuscu to immunize children against diphth tetanus, and pertussis.

DTaP v. A preparation of diphtl and tetanus toxoids and acellular pe sis proteins. It may be used for the fo and fifth injections in the series.

Haemophilus influenzae type b vaccine prepared from the bacterial saccharide (HbPV) or polysaccharide verted to protein (HbCV).

hepatitis B v. A vaccine prepared hepatitis B protein antigen produce genetically engineered yeast.

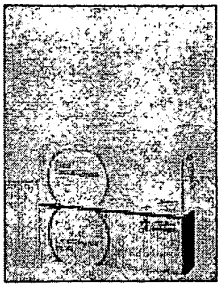
heterologous v. A vaccine derived an organism different from the orga against which the vaccine is used.

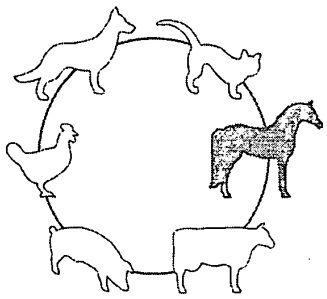
homologous v. Autogenous v.

human diploid cell rabies v. A HDCV. An inactivated virus vaccine pared from fixed rabies virus grown i man diploid cell tissue culture.

inactivated poliovirus v. An inject vaccine made from three types of in vated polioviruses. Previously used n poliomyelitis vaccine. SYN: *Salk v.*

influenza virus v. A polyvalent vac containing inactivated antigenic vari of the influenza virus (types A and ther individually or combined) for u areas expected to have epidemics. Its





Insol® Dermatophyton

Inactivated dermatophytosis vaccine

Dermatophytosis is the contagious superficial infection of the skin caused by dermatophytes (ringworm or tinea) and it is the most common skin disease in horses. The spores can survive for years.
Insol(r) Dermatophyton contains highly immunogenic strains of fungus. Based on a special manufacturing process the inactivated microconidia stimulate cell-mediated immune response in particular.
Insol(r) Dermatophyton contains no adjuvants, adsorbents, additives or excipients.

Indications

Active immunisation of horses, dogs, cats, rabbits and guinea pigs against dermatophytosis caused by trichophyton verrucosum, trichophyton mentagrophytes, trichophyton sarkisovii, trichophyton equinum, microsporum canis, microsporum gypseum and for the treatment of animals infected by dermatophytosis caused by these fungal species.

Features

- First vaccine against dermatophytosis in horses
- Covers all relevant strains
- For prophylaxis and therapy
- Easy application/handling

Benefits

- Comfortable way to combat dermatophytosis
- Safe for humans, safe for animals
- Vaccination during incubation possible
- 12 months protection appropriate for long term disease control

Presentation and mode of administration

Available in 5 x 2 ml glass vials for injection
For both prophylactic and therapeutic use 2 intramuscular injections 14 days apart on alternate sides of the body:

- horse <400 kg b.w.: 0.3 ml;
  400 - 600 kg b.w.: 0.5 ml; >600 kg b.w.: 0.7 ml
- dogs <10 kg b.w.: 0.3 ml; 10 - 40 kg b.w.: 0.5 ml;
  >40 kg b.w.: 1.0 ml
- cats <1 kg b.w.: 0.5 ml; >1 kg b.w.: 1.0 ml
- rabbits <3 kg b.w.: 0.5 ml; >3 kg b.w.: 1.0 ml
- guinea pigs: per 100 g b.w.: 0.1 ml

repeat vaccination at yearly intervals.

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Insol® Dermatophyton

Suspension

Für Tiere

Zusammenfassung der Produkteigenschaften

Bei jeder Injektion sollte die Körperseite gewechselt werden.
Zur Aufrechterhaltung des Impfschutzes sollten Wiederholungsbehandlungen nach prophylaktischer bzw. therapeutischer Anwendung in Form von zwei Impfungen im Abstand von 14 Tagen alle 10 bis 12 Monate erfolgen.

5.8 Überdosierung
Eine Überdosierung kann zu einer Verstärkung der aufgeführten Nebenwirkungen führen.

5.9 Besondere Warnhinweise für die Zieltierarten
keine

5.10 Wartezeit
Essbare Gewebe vom Pferd: 3 Tage

5.11 Besondere Vorsichtsmaßnahmen für Personen bei der Anwendung des Produktes
keine
Im Falle eines versehentlichen Verschüttens des Impfstoffes auf die Haut ist diese mit Wasser abzuwaschen.
Versehentliche Selbstinjektion kann zu vorübergehenden Schwellungen an der Injektionsstelle führen. In Fällen schwerer Nebenwirkungen nach versehentlicher Selbstinjektion mit dem Impfstoff sollte ein Arzt aufgesucht werden.

6. Pharmazeutische Daten

6.1 Unverträglichkeiten
Bezüglich möglicher Inkompatibilitäten wurden keine Studien durchgeführt.
Der Impfstoff darf nicht mit anderen Impfstoffen gemischt werden.

6.2 Haltbarkeit
Im ungeöffneten Behältnis:
36 Monate bei einer Lagerung zwischen +2°C bis +8°C
Im geöffneten Behältnis:
14 Tage bei einer Lagerung zwischen +2°C bis +8°C, sofern die Entnahmen ordnungsgemäß erfolgen.

6.3 Hinweise zur Aufbewahrung
Der Impfstoff ist zwischen +2°C und +8°C zu lagern!
Nicht einfrieren! Vor Licht schützen!
Impfstoff für Kinder unzugänglich aufbewahren!

6.4 Behältnis
2 ml-, 5 ml-, oder 10 ml-Glasflaschen der Glasart I, verschlossen mit Brombutyl-Gummistopfen und Aluminium-Bördelkappen

6.5 Zulassungsinhaber
Boehringer Ingelheim
Vetmedica GmbH
55216 Ingelheim

Hersteller
Serumwerk Memsen
27318 Hoyerhagen

6.6 Besondere Hinweise für die Beseitigung von unbrauchbarem Material
Leere Behälter, nicht völlig aufgebrauchter oder nach Ablauf des Verfalldatums nicht mehr verwendbarer Impfstoff sind unschädlich zu beseitigen.

7. Weitere Informationen

Zulassungs-Nummer: 1182/96

Datum der Genehmigung dieser Zusammenfassung der Produkteigenschaften:
24.01.2000

Abgabestatus: Verschreibungspflichtig

Zugelassene Handelsformen:
Packung mit 2 ml
Packung mit 5 x 2 ml

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim am Rhein
Telefon 0 18 03 / 660 660

Boehringer Ingelheim

311/0010

1. Name

Insol® Dermatophyton

2. Zusammensetzung

1 ml der inaktivierten Vakzine enthält jeweils mind. $6{,}25 \times 10^{5,0}$ Mikrokonidien der folgenden Pilzstämme:
- Trichophyton verrucosum, Stamm Nr. 410
- Trichophyton mentagrophytes, Stamm Nr. 1032
- Trichophyton sarkisovii, Stamm Nr. 551
- Trichophyton equinum, Stamm Nr. 381
- Mikrosporum canis, Stamm Nr. 1393
- Mikrosporum canis var. distortum, Stamm Nr. 120
- Mikrosporum canis var. obesum, Stamm Nr. 1311
- Mikrosporum gypseum, Stamm Nr. 59

und maximal 0,044 mg Thiomersal in einer Glucose-Fleischextrakt-Suspension.

3. Darreichungsform

Suspension zur Injektion

4. Immunologische Eigenschaften

Die Verabreichung des Impfstoffes bewirkt die Ausbildung einer Immunität bei Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophytosen, verursacht durch Trichophyton verrucosum, Trichophyton mentagrophytes, Trichophyton sarkisovii, Trichophyton equinum, Mikrosporum canis und Mikrosporum gypseum.

Die im Impfstoff enthaltenen Stämme sind tierischen Ursprungs: Trichophyton verrucosum (Stamm Nr. 410) wurde von einem Rentier, Trichophyton mentagrophytes (Stamm Nr. 1032) von einem Pferd, Trichophyton sarkisovii (Stamm Nr. 551) von einem Kamel, Trichophyton equinum (Stamm Nr. 381) von einem Pferd, Mikrosporum canis (Stamm Nr. 1393) von einer Katze, Mikrosporum canis var. distortum (Stamm Nr. 120) von einem Schwarzen Panther, Mikrosporum canis var. obesum (Stamm Nr. 1311) von einem Tiger und Mikrosporum gypseum (Stamm Nr. 59) von einem Pferd isoliert.

Die erzeugte Immunität ist hauptsächlich eine zell-vermittelte Immunantwort und hält in der Regel 10 bis 12 Monate an.

5. Klinische Daten

5.0 **Zieltierarten**
Pferde, Hunde, Katzen, Kaninchen und Meerschweinchen.

5.1 **Anwendungsgebiete**
Zur aktiven Immunisierung von Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophytosen, verursacht durch Trichophyton verrucosum, Trichophyton mentagrophytes, Trichophyton sarkisovii, Trichophyton equinum, Mikrosporum canis und Mikrosporum gypseum zum Zwecke der Reduktion des Risikos einer klinischen Infektion durch diese Pilzarten, sowie als therapeutische Maßnahme zur Beschleunigung der Abheilung der klinisch sichtbaren Hautveränderungen bei Tieren, die an einer durch diese Pilzarten verursachten Dermatophytose erkrankt sind.

5.2 **Gegenanzeigen**
Tiere mit Fieber und/oder mit dermatophytosenunabhängigen Symptomen einer infektiösen Erkrankung, sowie Tiere, die unter Kortikoid-Wirkung stehen, sollten nicht geimpft werden.
Jungtiere entsprechend den folgenden Angaben sind von einer Impfung auszuschließen:
Pferde unter 5 Monaten
Hunde unter 6 Wochen
Katzen unter 1 Monat
Kaninchen unter 6 Wochen
Meerschweinchen unter 150 g
Nicht geimpft werden dürfen gestresste Tiere, z.B. Pferde im Auktionsstress.

Insol® Dermatophyton
Zusammenfassung der Produkteigenschaften

5.3 **Nebenwirkungen**
Nach der Injektion können, besonders bei Pferden, bis zu hühnereigroße Schwellungen an der Injektionsstelle auftreten, die innerhalb von 3 bis 5 Tagen ohne weitere therapeutische Maßnahmen abheilen. In Einzelfällen wurden schmerzhafte, bis zu handflächengroße Schwellungen an der Injektionsstelle in Verbindung mit gestörtem Allgemeinbefinden (z.B. Fieber, Inappetenz, Apathie) beobachtet, die innerhalb von 8 bis 10 Tagen abgeklungen waren. In solchen Fällen ist eine symptomatische Behandlung zu empfehlen, wobei von lokal reizenden Mitteln abgesehen werden sollte.

5.4 **Besondere Hinweise für den Gebrauch**
Bei Tieren, die sich zum Zeitpunkt der Impfung im Inkubationsstadium befinden, kann es trotz Impfung zum Ausbruch der Erkrankung kommen. Die Hautveränderungen heilen jedoch innerhalb von 2 bis 4 Wochen nach 2. Injektion ab.
Da sich auch im Haarkleid der Tiere Dermatophytose-Erreger befinden können und diese durch die Impfung nicht erreicht werden, ist das Zoonosen-Risiko durch die Impfung zwar deutlich verringert, aber nicht vollständig auszuschließen. Aus diesem Grunde, sowie auch zur Senkung des Infektionsdruckes, ist bei langhaarigen Tieren das Scheren der Haare zu empfehlen. Aus dem gleichen Grunde wird empfohlen, auch solche Tiere zu impfen, die in direktem oder indirektem Kontakt zu infizierten Tieren stehen.
Zur Reduktion des allgemeinen Infektionsdruckes sollten außerdem Reinigungs- und Desinfektionsmaßnahmen der Umgebung sowie der Gebrauchsgegenstände (z.B. Putzzeug) durchgeführt werden.
Erfahrungen aus der Praxis haben gezeigt, dass insbesondere in Edelkatzenbeständen, in denen ein erhöhter Infektionsdruck zu erwarten ist, eine verminderte Wirksamkeit auftreten kann bzw. eine Rezidivneigung beobachtet werden kann.

5.5 **Anwendung während Trächtigkeit und Laktation**
Aufgrund des Manipulationsstresses stellen Impfungen zu Beginn und gegen Ende der Trächtigkeit allgemein ein Risiko dar und sollten deshalb vermieden werden.

5.6 **Wechselwirkungen**
Studien zu möglichen Wechselwirkungen wurden nicht durchgeführt.
Es wird jedoch empfohlen, zwischen den Impfungen, sowie innerhalb von 14 Tagen vor und nach den Impfungen keine anderen Immunisierungen vorzunehmen.

5.7 **Dosierung und Art der Anwendung**
Vor Gebrauch gut schütteln!
Die Impfdosis beträgt für
Pferde:
unter 400 kg KGW 0,3 ml
400–600 kg KGW 0,5 ml
über 600 kg KGW 0,7 ml
Hunde:
bis 10 kg KGW 0,3 ml
10 bis 40 kg KGW 0,5 ml
über 40 kg KGW 1,0 ml
Katzen:
bis 1,0 kg KGW 0,5 ml
über 1,0 kg KGW 1,0 ml
Kaninchen:
bis 3,0 kg KGW 0,5 ml
über 3,0 kg KGW 1,0 ml
Meerschweinchen:
pro 100 g KGW 0,1 ml
Sowohl zur Prophylaxe als auch zur Therapie sind 2 intramuskuläre Injektionen im Abstand von 14 Tagen erforderlich.
Ist bei an einer Dermatophytose erkrankten Tieren zwei Wochen nach zweiter Injektion noch keine eindeutige Verbesserung der Haut- und Haardefekte erkennbar, wird eine dritte Injektion empfohlen.
Auf eine strenge intramuskuläre Injektion ist zu achten; eine subkutane Injektion ist unbedingt zu vermeiden.

LM

Insol® Trichophyton

Boehringer Ingelheim

Inactivated trichophytosis vaccine for cattle

Aqueous suspension for intramuscular injection

Composition

1 ml of inactivated vaccine contains:
at least 17 x $10^{6.0}$ microconidia of each of the following strains of fungi:
- Trichophyton verrucosum, strain no. 410
- Trichophyton mentagrophytes, strain no. 1032
- Trichophyton sarkisovii, strain no. 551

and a maximum of 0.040 mg thimerosal
in a glucose meat extract suspension

Indications

Active immunisation of cattle from the age of 1 month onwards against trichophytosis caused by Trichophyton verrucosum, Trichophyton mentagrophytes and/or Trichophyton sarkisovii and as an aid in the treatment of cattle infected by trichophytosis caused by these fungal species.

Contraindications

None.

Undesirable effects

Slight swelling can occur at the injection site (mostly after accidental subcutaneous injection) which clears with no adverse symptoms.
In exceptional cases (ca. 0.05%) shock reactions in the form of dyspnoea, pulmonal oedema, reddish foam around the mouth and nose and heavy transpiration can occur (death can occur in ca. 0.01% of the vaccinated animals). In such cases symptomatic treatment including administration of adrenalin, glucocorticoids and antihistamines, possibly together with a dose of calcium, is indicated.

Special Precautions for use

In the case of animals which are in the incubation phase at the time of vaccination, the disease can still break out in spite of the vaccination. However, the skin lesions heal 2–4 weeks after the second injection.

Use during pregnancy and lactation

The vaccination can be carried out at any stage of pregnancy. To date no effect on milk output has been observed.

Interactions

No interaction studies have been performed.

However, it is recommended that no other immunisations be carried out between the vaccinations or within 14 days before and after the vaccinations.

Posology and method of administration

Shake well before use.

The vaccination dose is
for cattle with less than 70 kg bodyweight: 2.5 ml

for cattle with more than 70 kg bodyweight: 5.0 ml

ueous suspension for intramuscular
ection.
ase follow instructions carefully.
nl of inactivated vaccine contains:
least 17 x $10^{6.0}$ microconidia of each
the following strains of fungi:
Trichophyton verrucosum,
strain no. 410
Trichophyton mentagrophytes,
strain no. 1032
Trichophyton sarkisovii,
strain no. 551
d a maximum of 0.040 mg thimerosal
a glucose meat extract suspension

Withdrawal Periods:
Edible Tissue: 3 days
Milk: none

Storage:
Store at between +2°C and +8°C.
Do not freeze. Protect from light.
Once the bottle has been opened, the vaccine may be used for up to 14 days if extracted properly and stored in a cool place.

FOR ANIMAL TREATMENT ONLY
KEEP OUT OF REACH OF CHILDREN

Authorisation No: AR8/003/01

Boehringer Ingelheim Limited.
Ellesfield Avenue, Bracknell
Berks., RG12 8YS

9038
V 10153/IE/1

Batch No.:

Expiry Date:

LM
Insol® Trichophyton
Inactivated trichophytosis vaccine for cattle
100 ml
Boehringer Ingelheim

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Batch No.:

Expiry Date:

LM
Insol® Trichophyton
Inactivated trichophytosis vaccine for cattle
100 ml
Boehringer Ingelheim

Both for prophylaxis and for therapy 2 intramuscular injections with a 14-day interval are required. The injections should be given on alternate sides of the body. To maintain the vaccine protection after prophylactic or therapeutic administration, repeat vaccinations should be carried out at yearly intervals.

Subcutaneous injection is to be avoided

Overdose
Can lead to slight local intolerance reactions.

Special warnings for the target species
Animals with fever and/or symptoms of an infectious disease other than trichophytosis and animals which are still under the influence of corticosteroids should not be vaccinated. Animals under 4 weeks of age should not be vaccinated. Do not vaccinate stressed animals, for example animals for which a new strawbedding has been freshly prepared.

Withdrawal periods
Edible tissue: 3 days
Milk: none

Special precautions to be taken by the person administering the product to animals
None.

Rinse with water if the vaccine is accidentally spilled onto the skin. Accidental self injection may lead to mild transient swelling at the injection site. In case of severe side effects following an accidental self injection of vaccine a medical surgeon should be consulted.

Incompatibilities
No incompatibility studies have been performed.

St rage
Store at between +2°C and +8°C.
Do not freeze. Protect from light.

If stored at between +2°C and +8°C and as long as the vaccine is removed from the vial correctly, the vaccine may be used for up to 14 days after the vial has been opened.

Pack sizes
50 ml, 100 ml or 250 ml glass vials.

Warnings
For animal treatment only.
Keep vaccine out of the reach of children.
Do not use vaccine after the expiry date.
Empty containers and vaccine which is no longer usable after the expiry date are to be disposed of safely according to national requirements.

Manufacturer
Serumwerke Memsen
D-27318 Hoyerhagen
Germany

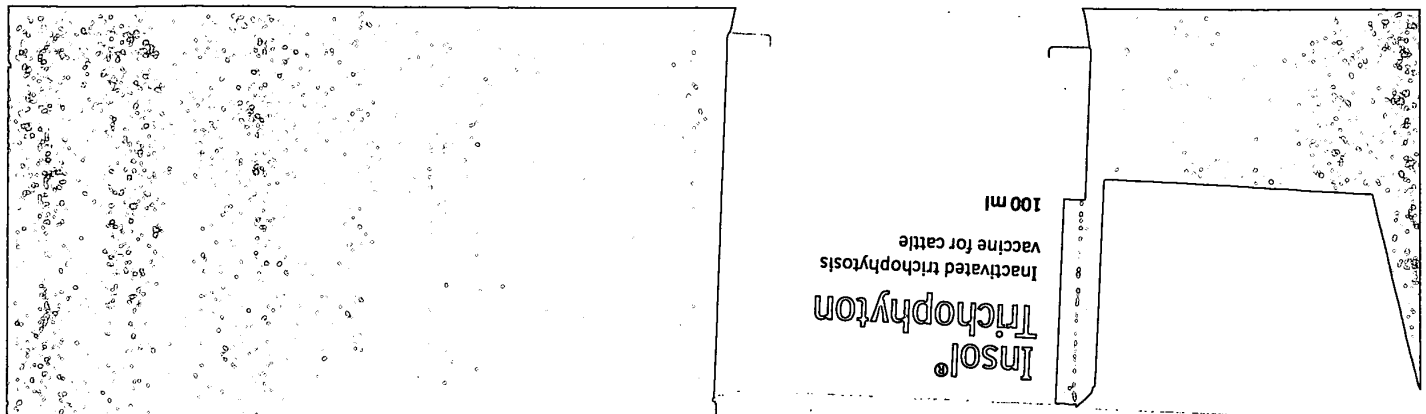
Authorisation No. AR8/003/01

Boehringer Ingelheim Limited
Ellesfield Avenue
Bracknell, Berkshire
RG12 8YS

V 10154/IE/1

This leaflet was written in March 1998.

9038



LM

Insol® Trichophyton

Inactivated trichophytosis vaccine for cattle

100 ml

Withdrawal Periods:

Edible Tissue:	3 days
Milk:	none

Storage:
Store at between +2°C and +8°C. Do not freeze. Protect from light. Once the bottle has been opened, the vaccine may be used for up to 14 days if extracted properly and stored in a cool place.

FOR ANIMAL TREATMENT ONLY
KEEP OUT OF REACH OF CHILDREN

AUTHORISATION NO: AR8/003/01

Boehringer Ingelheim

Boehringer Ingelheim Limited
Ellesfield Avenue, Bracknell
Berks., RG12 8YS

[redacted]

LM

Insol® Trichophyton

Inactivated trichophytosis vaccine for cattle

100 ml

Boehringer Ingelheim

5 012917 021004

Batch No.:

Expiry Date:

Aqueous suspension for intramuscular injection.
Please follow instructions carefully.

1 ml of inactivated vaccine contains:
at least $17 \times 10^{6.0}$ microconidia of each of the following strains of fungi:
- Trichophyton verrucosum, strain no. 410
- Trichophyton mentagrophytes, strain no. 1032
- Trichophyton sarkisovii, strain no. 551

and a maximum of 0.040 mg thimerosal
in a glucose meat extract suspension

9038

V 10155/IE/1

APPLICANT(S):	Polyakov, I. et al
SERIAL NO.:	10/085,703
CONFIRMATION NO.:	2400
FILING DATE:	February 28, 2002
DOCKET NO.:	3/400-4-C4
TITLE:	Dermatomycosis Vaccine

IN CONNECTION WITH THE ABOVE CASE, PLEASE DATE STAMP TO ACKNOWLEDGE RECEIPT OF THE DOCUMENTS LISTED BELOW, AND RETURN TO ADDRESSEE.

1. Brief On Appeal From The Primary Examiner's Decision To The Board Of Patent Appeals And Interferences (3 Originals)
2. Exhibits A, B, C, D and E

Mailed: August 15, 2003

V

V **1.** *Vibrio; vision; visual acuity.* **2.** Symbol for the element vanadium.

V̇ **1.** Symbol for gas flow. **2.** Symbol for ventilation.

v L. *vena*, vein; *volt*.

vaccina (văk-sī'nă) Vaccinia.

vaccinable (văk-sĭn'ă-b'l) Capable of being successfully vaccinated.

vaccinal (văk'sĭn-ăl) Rel. to vaccine or to vaccination.

vaccinate (văk'sĭn-āt) [L. *vaccinus*, pert. to cows] To inoculate with vaccine to produce immunity against disease.

vaccination (văk"sĭ-nā'shŭn) [L. *vaccinus*, pert. to cows] **1.** Inoculation with any vaccine or toxoid to establish resistance to a specific infectious disease. SEE: *immunization*. **2.** A scar left on the skin by inoculation of a vaccine.

vaccine (văk'sēn, văk-sēn') [L. *vaccinus*, pert. to cows] A suspension of infectious agents, or some part of them, given for the purpose of establishing resistance to an infectious disease. SEE: table.

Vaccines comprise four general classes:

1. Those containing living attenuated infectious organisms, such as vaccine for poliomyelitis.
2. Those containing infectious agents killed by physical or chemical means, such as vaccines used to protect human beings against typhoid fever, rabies, and whooping cough.
3. Those containing soluble toxins of microorganisms, sometimes used as such, but generally forming toxoids, such as the one used in the prevention of diphtheria and tetanus.
4. Those containing substances extracted from infectious agents, such as capsular polysaccharides extracted from pneumococci.

FUNCTION: Vaccines are used to stimulate an immune response in the body by creating antibodies or activated T lymphocytes capable of controlling the organism. The result is protection against a disease; the duration depends on the particular vaccine. Recovery from measles or diphtheria, for example, usually provides lifelong immunity. The immune system has produced antibodies and memory cells for these pathogens so that subsequent exposure does not result in disease. A successful vaccine does the same thing, usually without risk of illness. The measles vaccine is believed to provide lifelong immunity, but the diphtheria vaccine requires periodic booster doses. More than one type of vaccine may be available for immunization against a specific infectious agent. SEE: *diphtheria; immune response; immunity; immu tion; immunobiologics.*

autogenous v. Bacterial vaccine pared from lesions of the individual inoculated. SYN: *homologous v.*

bacterial v. A suspension of killed tenuated bacteria; used for injection the body to induce development of a immunity to the same organism.

BCG v. Bacille Calmette-Guéri preparation of a dried, living cultu *Mycobacterium tuberculosis*. In a with a high incidence of tuberculosis used in prophylactic vaccination o fants against tuberculosis. It is also in adults who are at high and unavoid risk of becoming infected with tuber sis. A disadvantage of use of this vac is that it produces hypersensitivity t berculin. As a result, the skin test fo berculin sensitivity becomes positive may persist for 5 years. There is no to distinguish a positive skin test d BCG from one caused by infection *Mycobacterium tuberculosis*.

cholera v. A vaccine prepared killed *Vibrio cholerae*. It is effective only a few months.

diphtheria v. SEE: *DPT v.*

DPT v. A combination of diphtheria tetanus toxoids and killed pertussis cilli that is administered intramuscul to immunize children against diphth tetanus, and pertussis.

DTaP v. A preparation of diphth and tetanus toxoids and acellular per sis proteins. It may be used for the fo and fifth injections in the series.

Haemophilus influenzae type b vaccine prepared from the bacterial p saccharide (HbPV) or polysaccharide verted to protein (HbCV).

hepatitis B v. A vaccine prepared f hepatitis B protein antigen produce genetically engineered yeast.

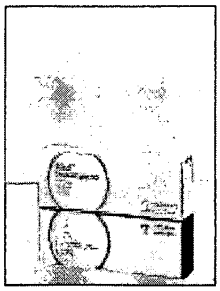
heterologous v. A vaccine derived f an organism different from the organ against which the vaccine is used.

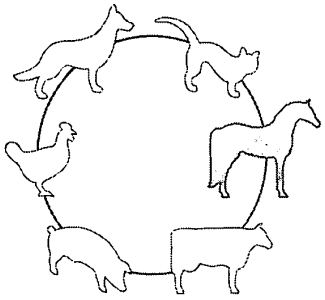
homologous v. Autogenous v.

human diploid cell rabies v. AB HDCV. An inactivated virus vaccine pared from fixed rabies virus grown in man diploid cell tissue culture.

inactivated poliovirus v. An injecta vaccine made from three types of ina vated polioviruses. Previously used na poliomyelitis vaccine. SYN: *Salk v.*

influenza virus v. A polyvalent vac containing inactivated antigenic varia of the influenza virus (types A and B ther individually or combined) for us areas expected to have epidemics. Its





Insol® Dermatophyton

Inactivated dermatophytosis vaccine

Dermatophytosis is the contagious superficial infection of the skin caused by dermatophytes (ringworm or tinea) and it is the most common skin disease in horses. The spores can survive for years.
Insol(r) Dermatophyton contains highly immunogenic strains of fungus. Based on a special manufacturing process the inactivated microconidia stimulate cell-mediated immune response in particular.
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Features

- First vaccine against dermatophytosis in horses
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- For prophylaxis and therapy
- Easy application/handling

Benefits

- Comfortable way to combat dermatophytosis
- Safe for humans, safe for animals
- Vaccination during incubation possible
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For both prophylactic and therapeutic use 2 intramuscular injections 14 days apart on alternate sides of the body:

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  400 - 600 kg b.w.: 0.5 ml; >600 kg b.w.: 0.7 ml
- dogs <10 kg b.w.: 0.3 ml; 10 - 40 kg b.w.: 0.5 ml;
  >40 kg b.w.: 1.0 ml
- cats <1 kg b.w.: 0.5 ml; >1 kg b.w.: 1.0 ml
- rabbits <3 kg b.w.: 0.5 ml; >3 kg b.w.: 1.0 ml
- guinea pigs: per 100 g b.w.: 0.1 ml

repeat vaccination at yearly intervals.

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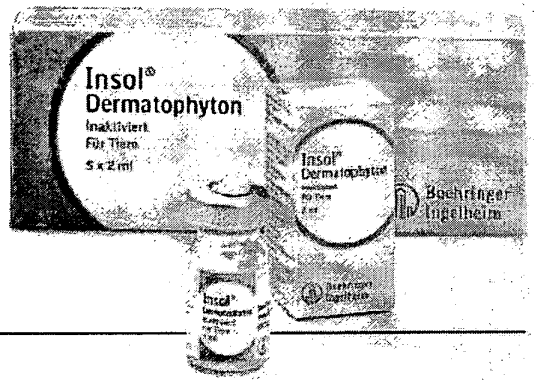
Insol® Dermatophyton

Suspension

Für Tiere

Zusammenfassung der Produkteigenschaften



Bei jeder Injektion sollte die Körperseite gewechselt werden.
Zur Aufrechterhaltung des Impfschutzes sollten Wiederholungsbehandlungen nach prophylaktischer bzw. therapeutischer Anwendung in Form von zwei Impfungen im Abstand von 14 Tagen alle 10 bis 12 Monate erfolgen.

5.8 Überdosierung
Eine Überdosierung kann zu einer Verstärkung der aufgeführten Nebenwirkungen führen.

5.9 Besondere Warnhinweise für die Zieltierarten
keine

5.10 Wartezeit
Essbare Gewebe vom Pferd: 3 Tage

5.11 Besondere Vorsichtsmaßnahmen für Personen bei der Anwendung des Produktes
keine
Im Falle eines versehentlichen Verschüttens des Impfstoffes auf die Haut ist diese mit Wasser abzuwaschen.
Versehentliche Selbstinjektion kann zu vorübergehenden Schwellungen an der Injektionsstelle führen. In Fällen schwerer Nebenwirkungen nach versehentlicher Selbstinjektion mit dem Impfstoff sollte ein Arzt aufgesucht werden.

6. Pharmazeutische Daten

6.1 Unverträglichkeiten
Bezüglich möglicher Inkompatibilitäten wurden keine Studien durchgeführt.
Der Impfstoff darf nicht mit anderen Impfstoffen gemischt werden.

6.2 Haltbarkeit
Im ungeöffneten Behältnis:
36 Monate bei einer Lagerung zwischen +2°C bis +8°C
Im geöffneten Behältnis:
14 Tage bei einer Lagerung zwischen +2°C bis +8°C, sofern die Entnahmen ordnungsgemäß erfolgen

6.3 Hinweise zur Aufbewahrung
Der Impfstoff ist zwischen +2°C und +8°C zu lagern!
Nicht einfrieren! Vor Licht schützen!
Impfstoff für Kinder unzugänglich aufbewahren!

6.4 Behältnis
2 ml-, 5 ml-, oder 10 ml-Glasfläschchen der Glasart I, verschlossen mit Brombutyl-Gummistopfen und Aluminiumbördelkappen

6.5 Zulassungsinhaber
Boehringer Ingelheim
Vetmedica GmbH
55216 Ingelheim

Hersteller
Serumwerk Memsen
27318 Hoyerhagen

6.6 Besondere Hinweise für die Beseitigung von unbrauchbarem Material
Leere Behälter, nicht völlig aufgebrauchter oder nach Ablauf des Verfalldatums nicht mehr verwendbarer Impfstoff sind unschädlich zu beseitigen.

7. Weitere Informationen

Zulassungs-Nummer: 118a/96

Datum der Genehmigung dieser Zusammenfassung der Produkteigenschaften:
24. 01. 2000

Abgabestatus: Verschreibungspflichtig

Zugelassene Handelsformen:
Packung mit 2 ml
Packung mit 5 x 2 ml

Boehringer Ingelheim Vetmedica GmbH
55216 Ingelheim am Rhein
Telefon 0 18 03 / 660 660

Boehringer Ingelheim

314/0010

1. Name

Insol® Dermatophyton

1. Zusammensetzung

1 ml der inaktivierten Vakzine enthält:
jeweils mind. $6{,}25 \times 10^{6,0}$ Mikrokonidien der folgenden Pilzstämme:

- Trichophyton verrucosum, Stamm Nr. 410
- Trichophyton mentagrophytes, Stamm Nr. 1032
- Trichophyton sarkisovii, Stamm Nr. 551
- Trichophyton equinum, Stamm Nr. 381
- Mikrosporum canis, Stamm Nr. 1393
- Mikrosporum canis var. distortum, Stamm Nr. 120
- Mikrosporum canis var. obesum, Stamm Nr. 1311
- Mikrosporum gypseum, Stamm Nr. 59

und maximal 0,044 mg Thiomersal in einer Glucose-Fleischextrakt-Suspension

3. Darreichungsform

Suspension zur Injektion

4. Immunologische Eigenschaften

Die Verabreichung des Impfstoffes bewirkt die Ausbildung einer Immunität bei Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophytosen, verursacht durch Trichophyton verrucosum, Trichophyton mentagrophytes, Trichophyton sarkisovii, Trichophyton equinum, Mikrosporum canis und Mikrosporum gypseum.

Die im Impfstoff enthaltenen Stämme sind tierischen Ursprungs: Trichophyton verrucosum (Stamm Nr. 410) wurde von einem Rentier, Trichophyton mentagrophytes (Stamm Nr. 1032) von einem Pferd, Trichophyton sarkisovii (Stamm Nr. 551) von einem Kamel, Trichophyton equinum (Stamm Nr. 381) von einem Pferd, Mikrosporum canis (Stamm Nr. 1393) von einer Katze, Mikrosporum canis var. distortum (Stamm Nr. 120) von einem Schwarzen Panther, Mikrosporum canis var. obesum (Stamm Nr. 1311) von einem Tiger und Mikrosporum gypseum (Stamm Nr. 59) von einem Pferd isoliert.
Die erzeugte Immunität ist hauptsächlich eine zell-vermittelte Immunantwort und hält in der Regel 10 bis 12 Monate an.

5. Klinische Daten

5.0 Zieltierarten
Pferde, Hunde, Katzen, Kaninchen und Meerschweinchen.

5.1 Anwendungsgebiete
Zur aktiven Immunisierung von Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophytosen, verursacht durch Trichophyton verrucosum, Trichophyton mentagrophytes, Trichophyton sarkisovii, Trichophyton equinum, Mikrosporum canis und Mikrosporum gypseum zum Zwecke der Reduktion des Risikos einer klinischen Infektion durch diese Pilzarten, sowie als therapeutische Maßnahme zur Beschleunigung der Abheilung der klinisch sichtbaren Hautveränderungen bei Tieren, die an einer durch diese Pilzarten verursachten Dermatophytose erkrankt sind.

5.2 Gegenanzeigen
Tiere mit Fieber und/oder mit dermatophytoseunabhängigen Symptomen einer Infektiösen Erkrankung, sowie Tiere, die unter Kortikoid-Wirkung stehen, sollten nicht geimpft werden. Jungtiere entsprechend den folgenden Angaben sind von einer Impfung auszuschließen:
Pferde unter 5 Monaten
Hunde unter 6 Wochen
Katzen unter 1 Monat
Kaninchen unter 6 Wochen
Meerschweinchen unter 150 g
Nicht geimpft werden dürfen gestresste Tiere, z.B. Pferde im Auktionsstress.

Insol® Dermatophyton
Zusammenfassung der Produkteigenschaften

5.3 Nebenwirkungen
Nach der Injektion können, besonders bei Pferden, bis zu hühnereigroße Schwellungen an der Injektionsstelle auftreten, die innerhalb von 3 bis 5 Tagen ohne weitere therapeutische Maßnahmen abheilen. In Einzelfällen wurden schmerzhafte, bis zu handflächengroße Schwellungen an der Injektionsstelle in Verbindung mit gestörtem Allgemeinbefinden (z.B. Fieber, Inappetenz, Apathie) beobachtet, die innerhalb von 8 bis 10 Tagen abgeklungen waren. In solchen Fällen ist eine symptomatische Behandlung zu empfehlen, wobei von lokal reizenden Mitteln abgesehen werden sollte.

5.4 Besondere Hinweise für den Gebrauch
Bei Tieren, die sich zum Zeitpunkt der Impfung im Inkubationsstadium befinden, kann es trotz Impfung zum Ausbruch der Erkrankung kommen. Die Hautveränderungen heilen jedoch innerhalb von 2 bis 4 Wochen nach 2. Injektion ab.
Da sich auch im Haarkleid der Tiere Dermatophytose-Erreger befinden können und diese durch die Impfung nicht erreicht werden, ist das Zoonosen-Risiko durch die Impfung zwar deutlich verringert, aber nicht vollständig auszuschließen. Aus diesem Grunde, sowie auch zur Senkung des Infektionsdruckes, ist bei langhaarigen Tieren das Scheren der Haare zu empfehlen. Aus dem gleichen Grunde wird empfohlen, auch solche Tiere zu impfen, die in direktem oder indirektem Kontakt zu infizierten Tieren stehen. Zur Reduktion des allgemeinen Infektionsdruckes sollten außerdem Reinigungs- und Desinfektionsmaßnahmen der Umgebung sowie der Gebrauchsgegenstände (z.B. Putzzeug) durchgeführt werden.
Erfahrungen aus der Praxis haben gezeigt, dass insbesondere in Edelkatzenbeständen, in denen ein erhöhter Infektionsdruck zu erwarten ist, eine verminderte Wirksamkeit auftreten kann bzw. eine Rezidivneigung beobachtet werden kann.

5.5 Anwendung während Trächtigkeit und Laktation
Aufgrund des Manipulationsstresses stellen Impfungen zu Beginn und gegen Ende der Trächtigkeit allgemein ein Risiko dar und sollten deshalb vermieden werden.

5.6 Wechselwirkungen
Studien zu möglichen Wechselwirkungen wurden nicht durchgeführt.
Es wird jedoch empfohlen, zwischen den Impfungen, sowie innerhalb von 14 Tagen vor und nach den Impfungen keine anderen Immunisierungen vorzunehmen.

5.7 Dosierung und Art der Anwendung
Vor Gebrauch gut schütteln!
Die Impfdosis beträgt für

Pferde:	
unter 400 kg KGW	0,3 ml
400 – 600 kg KGW	0,5 ml
über 600 kg KGW	0,7 ml
Hunde:	
bis 10 kg KGW	0,3 ml
10 bis 40 kg KGW	0,5 ml
über 40 kg KGW	1,0 ml
Katzen:	
bis 1,0 kg KGW	0,5 ml
über 1,0 kg KGW	1,0 ml
Kaninchen:	
bis 3,0 kg KGW	0,5 ml
über 3,0 kg KGW	1,0 ml
Meerschweinchen:	
pro 100 g KGW	0,1 ml

Sowohl zur Prophylaxe als auch zur Therapie sind 2 intramuskuläre Injektionen im Abstand von 14 Tagen erforderlich.
Ist bei an einer Dermatophytose erkrankten Tieren zwei Wochen nach zweiter Injektion noch keine eindeutige Verbesserung der Haut- und Haardefekte erkennbar, wird eine dritte Injektion empfohlen.
Auf eine strenge intramuskuläre Injektion ist zu achten; eine subkutane Injektion ist unbedingt zu vermeiden.

LM

Insol® Trichophyton

Boehringer Ingelheim

Inactivated trichophytosis vaccine for cattle

Aqueous suspension for intramuscular injection

Composition

1 ml of inactivated vaccine contains:
at least 17 x $10^{6.0}$ microconidia of each of the following strains of fungi:

- Trichophyton verrucosum, strain no. 410
- Trichophyton mentagrophytes, strain no. 1032
- Trichophyton sarkisovii, strain no. 551

and a maximum of 0.040 mg thimerosal
in a glucose meat extract suspension

Indications

Active immunisation of cattle from the age of 1 month onwards against trichophytosis caused by Trichophyton verrucosum, Trichophyton mentagrophytes and/or Trichophyton sarkisovii and as an aid in the treatment of cattle infected by trichophytosis caused by these fungal species.

Contraindications

None.

Undesirable effects

Slight swelling can occur at the injection site (mostly after accidental subcutaneous injection) which clears with no adverse symptoms.
In exceptional cases (ca. 0.05%) shock reactions in the form of dyspnoea, pulmonal oedema, reddish foam around the mouth and nose and heavy transpiration can occur (death can occur in ca. 0.01% of the vaccinated animals). In such cases symptomatic treatment including administration of adrenalin, glucocorticoids and antihistamines, possibly together with a dose of calcium, is indicated.

Special Precautions for use

In the case of animals which are in the incubation phase at the time of vaccination, the disease can still break out in spite of the vaccination. However, the skin lesions heal 2–4 weeks after the second injection.

Use during pregnancy and lactation

The vaccination can be carried out at any stage of pregnancy. To date no effect on milk output has been observed.

Interactions

No interaction studies have been performed.

However, it is recommended that no other immunisations be carried out between the vaccinations or within 14 days before and after the vaccinations.

Posology and method of administration

Shake well before use.

The vaccination dose is
for cattle with less than
70 kg bodyweight: 2.5 ml

for cattle with more than
70 kg bodyweight: 5.0 ml

ueous suspension for intramuscular
ection
ase follow instructions carefully

nl of inactivated vaccine contains
least 17 x $10^{6.0}$ microconidia of each
the following strains of fungi:
Trichophyton verrucosum,
strain no. 410
Trichophyton mentagrophytes,
strain no. 1032
Trichophyton sarkisovii,
strain no. 551
d a maximum of 0.040 mg thimerosal
a glucose meat extract suspension

Boehringer Ingelheim

LM
Insol® Trichophyton
Inactivated trichophytosis vaccine for cattle
100 ml

Withdrawal Periods
Edible Tissue 3 days
Milk none

Storage:
Store at between +2°C and +8°C
Do not freeze. Protect from light.
Once the bottle has been opened, the vaccine may be used for up to 14 days if extracted properly and stored in a cool place.

FOR ANIMAL TREATMENT ONLY
KEEP OUT OF REACH OF CHILDREN

Authorisation No: AR8/003/01

Boehringer Ingelheim Limited.
Ellesfield Avenue, Bracknell
Berks., RG12 8YS

9038
V 10153/IE/1

Batch No.:

Expiry Date:

ueous suspension for intramuscular
ection
ase follow instructions carefully

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Boehringer Ingelheim

LM
Insol® Trichophyton
Inactivated trichophytosis vaccine for cattle
100 ml

Withdrawal Periods:
Edible Tissue: 3 days
Milk: none

Storage:
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Do not freeze. Protect from light.
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FOR ANIMAL TREATMENT ONLY
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Ellesfield Avenue, Bracknell
Berks., RG12 8YS

9038
V 10153/IE/1

Batch No.:

Expiry Date:

Both for prophylaxis and for therapy 2 intramuscular injections with a 14-day interval are required. The injections should be given on alternate sides of the body. To maintain the vaccine protection after prophylactic or therapeutic administration, repeat vaccinations should be carried out at yearly intervals.

Subcutaneous injection is to be avoided

Overdose
Can lead to slight local intolerance reactions.

Special warnings for the target species
Animals with fever and/or symptoms of an infectious disease other than trichophytosis and animals which are still under the influence of corticosteroids should not be vaccinated. Animals under 4 weeks of age should not be vaccinated. Do not vaccinate stressed animals, for example animals for which a new strawbedding has been freshly prepared.

Withdrawal periods
Edible tissue: 3 days
Milk: none

Special precautions to be taken by the person administering the product to animals
None.

Rinse with water if the vaccine is accidentally spilled onto the skin. Accidental self injection may lead to mild transient swelling at the injection site. In case of severe side effects following an accidental self injection of vaccine a medical surgeon should be consulted.

Inc mpatibilities
No incompatibility studies have been performed.

Storage
Store at between +2°C and +8°C.
Do not freeze. Protect from light.

If stored at between +2°C and +8°C and as long as the vaccine is removed from the vial correctly, the vaccine may be used for up to 14 days after the vial has been opened.

Pack sizes
50 ml, 100 ml or 250 ml glass vials.

Warnings
For animal treatment only.
Keep vaccine out of the reach of children.
Do not use vaccine after the expiry date.
Empty containers and vaccine which is no longer usable after the expiry date are to be disposed of safely according to national requirements.

Manufacturer
Serumwerke Memsen
D-27318 Hoyerhagen
Germany

Authorisation No. AR8/003/01

Boehringer Ingelheim Limited
Ellesfield Avenue
Bracknell, Berkshire
RG12 8YS

This leaflet was written in March 1998.

V 10154/IE/1

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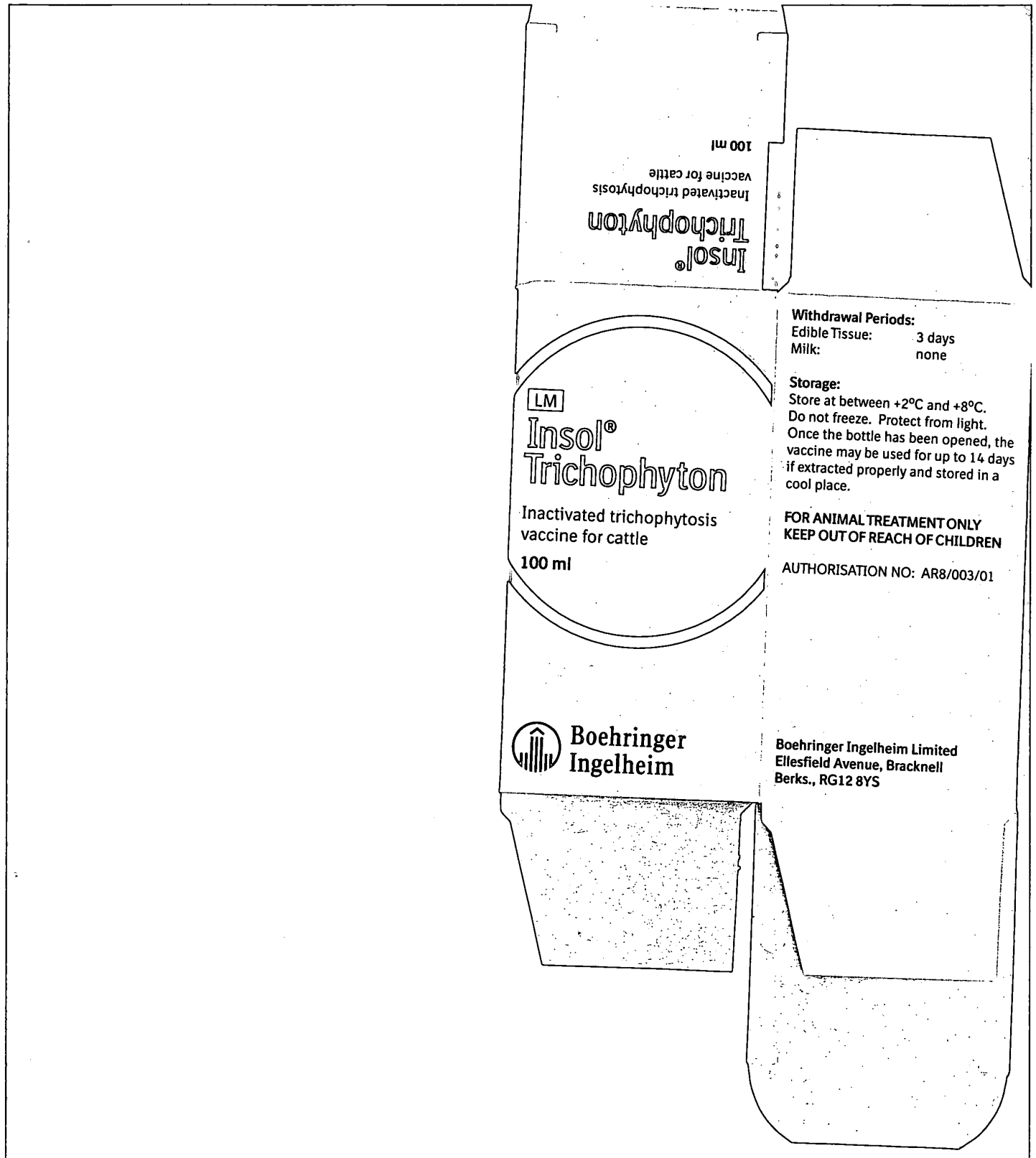
Insol®
Trichophyton
Inactivated trichophytosis
vaccine for cattle
100 ml
LM
Insol®
Trichophyton
Inactivated trichophytosis
vaccine for cattle
100 ml
Withdrawal Periods:
Edible Tissue: 3 days
Milk: none
Storage:
Store at between +2°C and +8°C.
Do not freeze. Protect from light.
Once the bottle has been opened, the vaccine may be used for up to 14 days if extracted properly and stored in a cool place.
FOR ANIMAL TREATMENT ONLY
KEEP OUT OF REACH OF CHILDREN
AUTHORISATION NO: AR8/003/01
Boehringer Ingelheim
Boehringer Ingelheim Limited
Ellesfield Avenue, Bracknell
Berks., RG12 8YS

LM

Insol® Trichophyton

Inactivated trichophytosis vaccine for cattle

100 ml

Boehringer Ingelheim

5 012917 021004

Batch No.: 894

Expiry Date: 08.07.2008

Aqueous suspension for intramuscular injection.
Please follow instructions carefully.

1 ml of inactivated vaccine contains:
at least 17 x $10^{6.0}$ microconidia of each of the following strains of fungi:
- Trichophyton verrucosum, strain no. 410
- Trichophyton mentagrophytes, strain no. 1032
- Trichophyton sarkisovii, strain no. 551

and a maximum of 0.040 mg thimerosal
in a glucose meat extract suspension

9038

V 10155/IE/1